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Editorial

Vectorcardiography

Pierre W. Duchosal, M.D., Geneva, Switzerland

Publications on research in the field of vectorcardiography, clinical and theoretical, have increased in number in the last years. Periodic controversy has also arisen as to whether the vectorcardiographic method is justified, useful, and correct. Vectorcardiography cannot be readily matched with electrocardiography, which was introduced so many years before, and which rests firmly on numerous well-established bases and on a tremendous clinical iconography. For these reasons a comparison is premature. On the other hand, it is illogical to place in competition procedures which, in fact, are complementary. It is often argued against vectorcardiography that the spatial vectorcardiographic loop cannot offer more than the three scalar electrocardiograms from which it originates. Such reasoning is not essentially wrong. It unfortunately presumes a highly developed mental process of which the mind is incapable. Transforming by imagination alone three coordinate values into their spatial resultant is a strenuous intellectual effort. When dealing with such changing coordinate values as three electrocardiograms, the mental process becomes impossible for most of us.

Having taken this first step in discussing vectorcardiography, we now need to evaluate the clinical interest in the method at present. What are the limits of validity of its concept? In other words, to what extent is the carrying out of such studies justified? The reply to this ingenuous question may be considered under the following three points:

1. The analytic concept of the electrocardiograms as inaugurated by Frank Wilson justifies, of itself, vectorcardiography. It seems, however, that according to the opinion expressed by several authors, an approximate estimation of the spatial vectors based on simple scalar leads may give satisfactory answers to most problems.

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2. Precordial leads which are supposed to behave like semidirect leads are influenced by local potentials from the closest part of the epicardium, which distort the general vector. Such influences would not appear in a distant VCG.

3. The ideal spatial VCG is not yet obtainable with sufficient accuracy to warrant a really precise and over-all picture of the electromotive forces. Too many lead systems of vectorcardiography, with differing results, have been proposed and confusion ensues, which is not encouraging for practical or routine application.

Point 1, regarding the simple and satisfactory picture of a vector estimated from ordinary scalar leads, is a temporary opinion. On the contrary, the modern electrophysiologic tendency is to dissect the myocardial electrogenesis into smaller and smaller elements.[15,21] The observation of details in vector analysis is not in disagreement with this attitude. This comparison between details of two different kinds deserves a comment. A distant lead vector results from a summation of several sources, without providing specific information in regard to their number and anatomic origin. This difficulty rarely prevented electrocardiographers from attempting a detailed electrogenic analysis of the vector. What this is worth for an ordinary ECG is as valid for the VCG. The latter, owing to its refined and more complete expression in three dimensions, certainly deserves as much interest as the former in such attempts.

Point 2 concerns local effects which are shown by semidirect leads but not distinctly by the vectorcardiogram. One is justified, however, in preferring a balanced and fully representative picture of the electromotive forces, even if local effects are poorly registered. The local influence on scalar leads also cannot be predicted nor estimated in intensity in respect to the over-all potentials. This influence is an occasional one, sometimes dominant, sometimes nil. When dominant, the local effect is expressed by additional vectors whose influence rapidly decreases with an increase in distance. This point is particularly adapted to those conditions in which electric forces from the myocardium near the electrode constitute the only, or most, active source of heart vectors at a given moment. A typical example is supplied by the injury currents of anterior wall infarction. An apparently paradoxical and reversed situation is realized when a local subtractive process is involved instead of an additive one. For example, at the time of depolarization, infarcted epicardial zones of the anterior wall close to a precordial electrode become inactive and deprive the recorded ECG of any local influence of their own. This affects the QRS part of the ventricular complex, but not by the mechanism of proximity. The intact parts of the myocardium beyond the injured area continue to exert their influence on the precordial electrode, but they are remote in comparison to the infarcted epicardial layer. This fact explains why QS-type complexes in Leads V_2 and V_3 have their counterpart on the back with an R pattern instead of a qR. This process is quite distinct on the spatial VCG, and to the same extent as it is present on the precordial or back leads.

Such a failure of the precordial leads to express local effects better than do the remote leads (the VCG is also remote) is a common finding. It is not an exaggeration to say that this finding is representative of the majority of normal

conditions and also of many pathologic ones: left ventricular hypertrophy, WPW syndrome, many different types of infarction, etc. Astonishing as it may be, this is a matter of fact. Recent experimental research[10] on the influence of proximity or distance on the ECG of an isolated cat's heart recorded in a volume conductor have permitted a better calibration of the effects of proximity. At a distance beyond one diameter of the heart, outside the epicardial surface, local effects are scarcely visible on unipolar electrocardiograms. The human conditions seem to be comparable, or better. Modern research work tending to prove that electrogenesis from the inner shell of the ventricles scarcely influences the peripheral ECG is not very well supported by the observations mentioned above. On the one hand, the precordial leads are representative of balanced, over-all electrical forces; on the other hand, it is supposed that these forces arise from the outer shell of the ventricles only. Would it not be more satisfactory to believe that just the contrary hypothesis is more applicable? This theoretical point is not advanced in opposition to the validity of the recent electrophysiologic discoveries. In order for there to be good agreement between the vectorcardiographic assessments and the recent physiologic thesis, there has to be an extraordinary symmetry in the centrifugal spread of the depolarization process. How otherwise can the excellent mirror pattern of myocardial infarction and the cancellations be explained?[20] Assuming that the inner shell is not electrically inert in regard to the peripheral ECG is partly supported by recent experiments.[18]

The concept of the intrinsicoid deflection is directly affected by the preceding considerations. Unless large epicardial surfaces display similar electrical patterns as predicted by Wilson, there is no chance to record equivalent electrocardiograms on the precordium. Recently published investigations[11] made during heart surgery have shown complete discrepancy between epicardial intrinsic time and the corresponding intrinsicoid deflection. The theoretical background of this problem is not questioned, but its application today no longer appears to be valid. The clear-cut distinction between precordial leads, as semidirect leads, and the limb leads, as remote leads, is no longer tenable. It is well established today that precordial leads most often display patterns entirely comparable in their over-all implication, as do the limb leads.

Point 3 is related to the technical problems of vectorcardiography. There is no fully satisfactory method for recording vectorcardiograms, which is sufficient reason to discourage the cardiologists who are not naturally attracted by vectorcardiography and who prefer to rely on the monumental and reliable data of classical electrocardiography. But it is by no means a deterrent to those who have spent so much of their time in improving the vectorcardiographic method and in giving more credit and reliability to its results.[3,6,9,12,17] Their efforts are about to overcome most of the former difficulties. Successive improvements by different teams have gradually provided a good standard.[3,6,8] Records nearly free from effects of eccentricity or proximity of the heart, and from hazardous conductivity interferences, are now obtainable. Mutual understanding will not fail to lead to a satisfactory agreement on a standard method among vectorcardiographers. In this respect, the systems based on correction coefficients are competing with the systems using external resistance nets and multiple electrodes.[16,17]

Numerous clinical applications have already been made based on different lead systems: trihedron of different types, the tetrahedron, and other combinations using Leads V_2, V_6, or Leads I and V_F, more or less calibrated. The tetrahedron method deserves special mention by reason of its direct relation to the classical standard leads in the frontal plane. Some authors[2] consider their interdependence as an advantage, not only in maintaining a close relationship between the two graphic expressions, but also in transferring the gains of the large

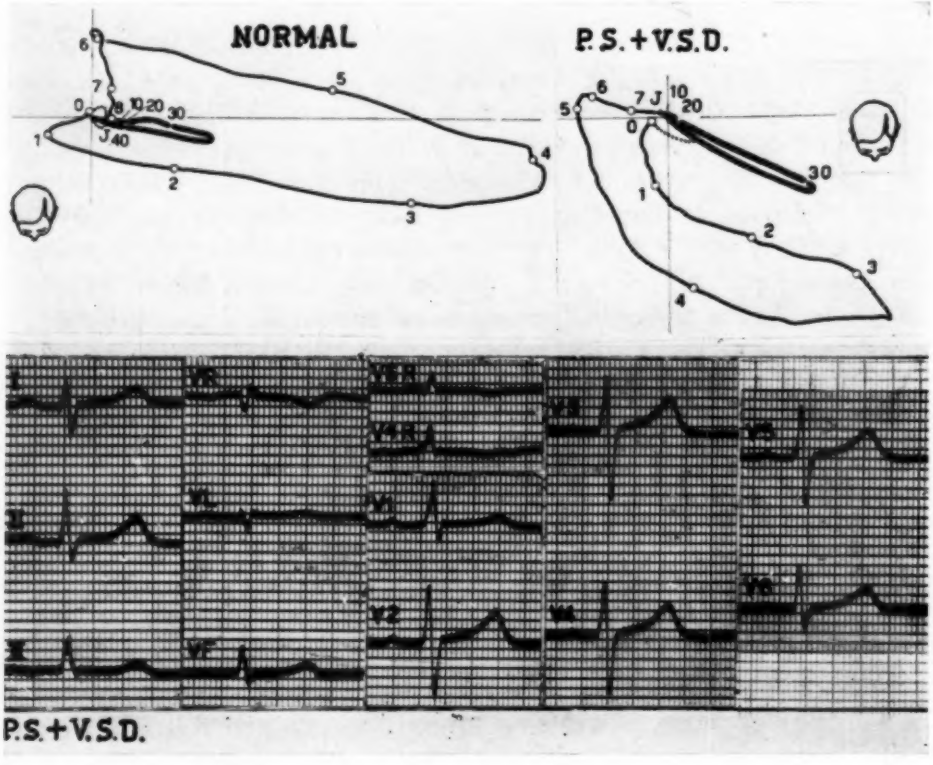

Fig. 1.—Example of a case in which the horizontal VCG shows more evidence of marked right ventricular hypertrophy than do the the scalar leads. Clinical diagnosis is infundibular pulmonary stenosis and interventricular septal defect. Right ventricular pressure is 108/1 mm. Hg; pulmonary artery pressure is 19/5 mm. Hg. Upper left: a normal horizontal VCG for comparison.

electrocardiographic experience into vectorcardiography. Others, including the author, do not attach so much importance to such a bridge and would prefer to consider the VCG as seen from a great distance. It seems that the tetrahedron is the least adapted method in this respect, as compared with the other lead systems mentioned above. Clinical application using different systems has already provided many interesting findings. Their diagnostic significance has been compared with electrocardiographic tracings. Vectorcardiograms have been used also to analyze critically the scalar pattern, normal or abnormal. A large number of the electrocardiographic concepts have been confirmed; a number are still subject to debate, as already discussed. Good agreement is found in the

material dealing with hypertrophy, block, and injuries. Right ventricular hypertrophy is often more apparent from vectorcardiograms than from electrocardiograms, but always better quantitatively assessed by the latter.[1,4,7] An example is shown in Fig. 1. The same is true for left ventricular hypertrophy, but to a lesser degree. The calculation of the QRS surface area adds reliable information.[13]

Incomplete bundle branch block, with its numerous and various scalar patterns, always raises questionable qualification. There is no doubt that in the long run a better classification in this complicated group will be clarified by vectorcardiography.

The normal VCG has been repeatedly described by several authors and methods. The latest studies[5,14] in this field have been more gratifying than the ones published in previous years. Normal individual variations account for the many scalar patterns. The variations in the different vectorcardiographic types affect the contour of the QRS-vector loop and its principal plane of orientation.

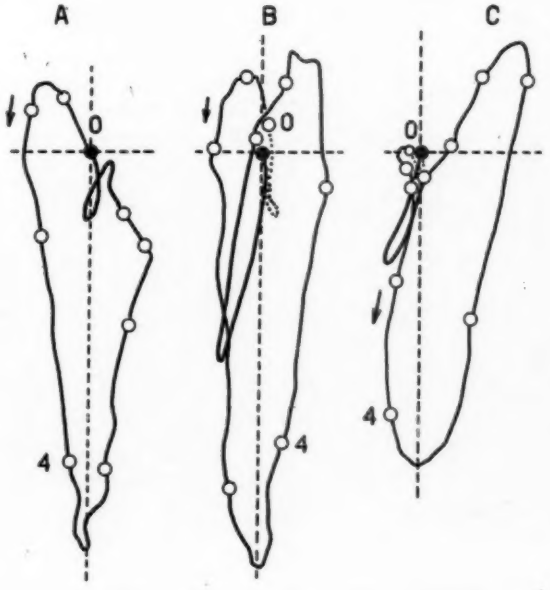

Fig. 2.—Semischematic representation of the three most frequent types of normal VCG, as viewed perpendicularly to their "plane of predilection." This "open view" shows definite variations in the initial and final portions of the loop. *A*, Initial shoulder well developed, final shoulder poorly developed. *B*, Initial and final shoulders equally and fairly well developed. *C*, Initial shoulder poorly developed, final shoulder widely developed. The spatial location of these three figures is not fixed except for their long axes, which are roughly parallel.

The vector loops may exhibit large or small initial or terminal appendages, or "shoulders" (Fig. 2). The body of the loop, also termed accelerated phase or portion, is narrow and more constant in proportion. The plane of predilection of the loop, defined as the contour during the accelerated phase, has a long axis which is very much alike in all normal subjects. This rare spatial dispersion of long axes of the loop is very typical of the normal VCG pattern. Usually it does not correspond with the scalar electrical axis, but agrees well with the anatomic axis. The discrepancy between the vectorcardiographic and electrocardiographic

axes is readily explained by extracardiac factors, especially the body build. Pyknic or slender individuals display unique relationships in the distance between the shoulders and between shoulders and thigh. Lead I is larger when Lead II is shorter and vice versa. This fact directly influences the amplitude of potentials in these leads, and consequently the electrical axis. This extrinsic factor is more responsible than the heart position itself for the complete disagreement between

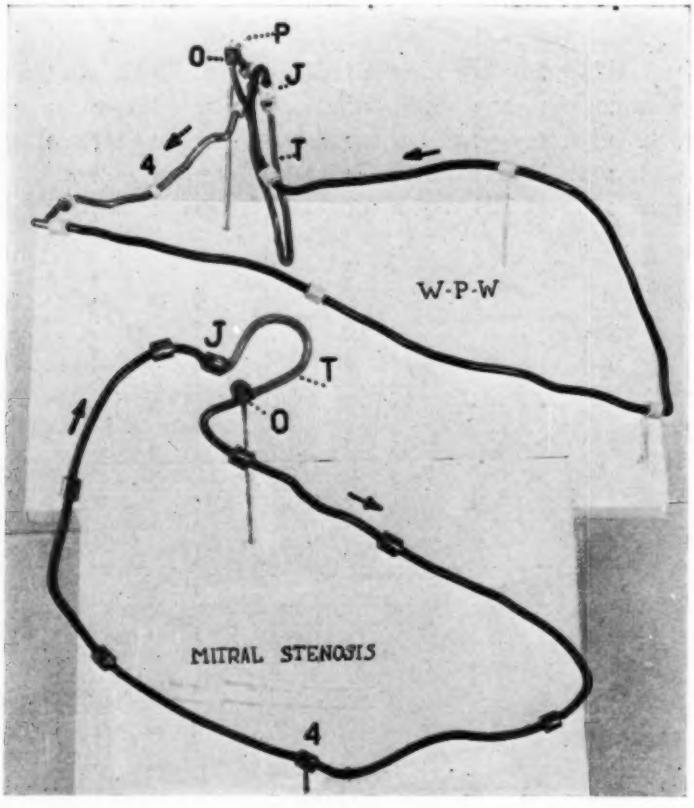

Fig. 3.—Two spatial vectorcardiograms, built as plastic models, representing two distinct cases: a WPW syndrome, above, and an advanced case of mitral stenosis, below. The models are viewed slightly from above in frontal incidence. Both QRS loops are markedly turned anteriorly. No force pointing to the back is observed except for the T wave in the mitral case. Both loops resemble each other in regard to their general contour and spatial location, but they are opposite in rotation (see arrows and time marks, 1/100 sec.). T loops are entirely different. The superior model shows large pre-excitation initial vectors, up to timing 6 (grey part of the QRS path), which are pointing forward and to the right, a centrifugal direction which is very rarely observed in any condition, including WPW syndrome.

heart axis and electrical axis from the scalar leads. It has been suspected that the concept of heart rotation, or apex displacement forward and backward, does not fit well with homologous anatomic variations.[19] Vectorcardiography affords consistent observations in the same sense and shows that the individual vector loop and the orientation of its open view are the main causes for variations in the normal patterns.[5,14] This point carries still more weight when applied to pathologic patterns.

Constructed wire models present striking pictures of the spatial development of electromotive forces as a whole and as a function of time. In medical teaching such models are wonderful tools for undergraduates, and for postgraduates as well. In the future there will certainly be special devices available for immediate and perfect stereoscopic visualization of the electrical cycle, completed by panoramic rotation. Two examples of typical pathologic stereovectorgraphic models are shown in Fig. 3, demonstrating the clarity of the spatial picture and making more convincing the valuable complement it represents.

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Correlation of the Precordial and Endocardial Ventricular Electrocardiogram

Janet Dickens, M.D., and Harry Goldberg, M.D.,** Philadelphia, Pa.*

INTRODUCTION

The discrepancies still apparent in electrocardiographic interpretation indicate the necessity for further studies of the activation of the human heart. Particular interest in the differentiation of right bundle branch block and right ventricular hypertrophy led us to employ the endocardial electrocardiographic technique in a large series of patients with congenital and acquired heart disease in an attempt to clarify their mechanism. Comparison, for possible diagnostic significance, of the endocardial tracings with the routine electrocardiograms, type of cardiac lesion, and physiologic data was made.

MATERIAL AND METHODS

Eight patients with normal cardiovascular systems and 42 with congenital and acquired cardiac lesions were studied. The diagnosis was made in all following cardiac catheterization in conjunction with the routine history, physical examination, chest x-ray, and electrocardiogram. Group I comprises 8 patients in whom no lesions were demonstrated by the above studies. In three, a diagnosis of idiopathic dilatation of the pulmonary artery was made. One patient was explored for a possible atrial septal defect. No lesions were found. In one patient a diagnosis of idiopathic right bundle branch block was made. Group II comprises 16 patients in whom a diagnosis of atrial septal defect was made. Closure of the defect by the atrioseptopexy technique was subsequently performed in 11. Group III includes 8 patients with ventricular septal defect, one of whom was operated upon. In Group IV are 2 patients with cardiopulmonary disease. A diagnosis of primary pulmonary hypertension was made in one, and bronchial asthma and pulmonary fibrosis in the other. Group V includes 4 patients with pure pulmonic stenosis. Pulmonary valvulotomy was subsequently performed in all, with pure valvular stenosis demonstrated in three and pure infundibular stenosis in the other one. One patient was studied 8 months postoperatively. Group VI comprises 6 patients with a diagnosis of tetralogy of Fallot. Four patients were operated upon and two were studied 3 and 5 years, respectively, following pulmonary valvulotomy. In both, significant pulmonary artery-right ventricular systolic pressure gradients and left-to-right shunts were still present. Valvular stenosis was demonstrated in three and infundibular stenosis in three. In Group VII are 6 patients with aortic stenosis, of whom five were

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*Assistant Director, Brith Sholom Cardiopulmonary Laboratory, Hahnemann Medical College and Hospital, Philadelphia, Pa.

**Assistant Professor, Department of Medicine, Hahnemann Medical College and Hospital of Philadelphia; Director, Brith Sholom Cardiopulmonary Laboratory, Hahnemann Medical College and Hospital of Philadelphia; and Cardiologist, Bailey Thoracic Clinic, Philadelphia, Pa.

operated upon and one was studied 3 years after aortic commissurotomy. In five patients left heart catheterization was performed and aortic systolic pressure gradients were demonstrated in all.

Right heart catheterization was performed in the usual manner employing a Cournand electrode catheter. The electrode tip was situated 1 mm. from the end of the catheter. Simultaneous recordings of the endocardial electrocardiogram, right heart pressures, and Lead V_{4R} or Lead II of the peripheral electrocardiogram were obtained. Endocardial leads were obtained in the pulmonary artery, right ventricular outflow, mid, and tricuspid areas, and in the low right atrium. Recordings were also made during pullback of the catheter across the pulmonic and tricuspid valves. Tracings were recorded on a photo-oscillographic unit* or polyoscillograph† with sensitivity adjusted so that 1 millivolt equaled 10 mm. of deflection. Known changes in sensitivity and paper speed were made, where necessary, for accurate study of the tracings.

Criteria for right ventricular hypertrophy were those of Sokolow and Lyon,[1] and for complete right bundle branch block, those of Wilson and associates.[2] Incomplete right bundle branch block was diagnosed by the criteria of Barker and Valencia.[3] Criteria for left ventricular hypertrophy were those of Sokolow and Lyon.[4]

RESULTS

Group I—No Cardiac Defects.—The data are shown in Table I. The electrocardiogram was considered within normal limits in all but one patient, D.D., in whom a diagnosis of idiopathic right bundle branch block was made. In another, C.H., incomplete right bundle branch block developed during the procedure.

In several patients more than one endocardial pattern was recorded at the same position, presumably due to movement of the catheter. In most patients, however, the tracings were consistent at each position.

While the patterns were variable in the main pulmonary artery, over the tricuspid valve, and in the low right atrium, an R′ or r′ was seen in 7 patients as the catheter approached the pulmonic valve, becoming more prominent in some patients or appearing for the first time in this position in others. In all, an R′, r′, or notch on the descending S of an rS pattern was recorded in the right ventricular outflow position (Fig. 1). An R′ was seen less frequently in the right ventricular tricuspid area, but was commonly observed over the tricuspid valve as an rsR′ or Qrs. In the mid right ventricle an rS or RS was the usual pattern. Persistence of an RSr′s′ complex in this position was seen only in patient D.D., with idiopathic right bundle branch block. In this patient also, an unusual and complex pattern, rsr′s′R″S″ and rsR′S′r″s″, was recorded over the pulmonic and tricuspid valves (Fig. 2).

Tracings obtained in patient C.H. who developed incomplete right bundle branch block were in no way different from those with normal electrocardiograms.

Group II—Atrial Septal Defect.—The data are shown in Table II*A*. The electrocardiogram was considered within normal limits in 1 patient. In 7 a diagnosis of right ventricular hypertrophy and strain was made. Five of the latter showed a qR complex in V_1, which persisted in V_2 in 1 patient and in V_{4R} in 2 patients. Eight patients with an rSr′ or rsR′ in V_1 met the established criteria for incomplete right bundle branch block.

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*Electronics for Medicine, White Plains, N. Y.
†Sanborn Company, 175 Wyman St., Waltham 54, Mass.

TABLE I. NORMAL SUBJECTS

PATIENT	ENDOCARDIAL LEADS							PRECORDIAL LEADS			
	MAIN PULMONARY ARTERY	PULMONIC VALVE	RIGHT VENTRICLE			TRICUSPID VALVE	LOW RIGHT ATRIUM	V_1	V_{4R}	RIGHT VENTRICULAR PRESSURE (MM. Hg)	AGE (YR.)
			OUTFLOW	MID	TRICUSPID						
J.T.	rSr′	rsR′S′	Rsr′S′ .11* r_nS	rS	rsr′S′	Qrs Q_nS	Qrs	rS	rS .10*	28/4	17
E.McI.	rSr′	rsR′S′	rsR′S′ .08 rS	rS	rS	0	rS^n	rS	rS .08	18/0	26
P.P.	rS^{sl}	RSr′S′	RSr′S′ .09	RS	rS	rS	QS	rS	rS .09	22/1	18
M.B.	rS	0	RSr′s′ .08	RS	rS	QRS	Qr QS	R_nS	rSr′ .07	20/2	12½
C.H.θ	rSr′s′	Rsr′S′	0	RS^{sl} .10	r_nS	rsR′S′	Q^nr	RS	qR .09	14/2	22 mo.
D.D.	rSr′s′	rSr′S′ rSr′s′R″S″	rsR′S′ .12 r_nS	RSR′s′φ RSr′s′	RSr′s′ rsR′Sr″s″	rsR′S′r″s″	QR	rsR′	rsR′ .12	33/2	14
E.Sh.	rS^n	rS^n RSr′s′	rsR′S′ .08 rsr′s′	rSφ	rS	RS	qrS	rS	rSr′ .08	25/1	20
R.H.	rS	rSr′S′ rSR′	Rsr′S′ .10	rS	rS	r_nS	r_nS QS_n	rS	rS .08	25/2	21

Symbols:

*QRS duration in seconds.
n subscript = notch on the descending limb.
n superscript = notch on the ascending limb.
sl superscript = slur on the ascending limb.
θ = right bundle branch block developed during the procedure.
φ = apex position.

In 14 patients in whom tracings were recorded as the catheter was withdrawn across the pulmonic valve, an R′ was seen in 9 and an r′ in 3. In 2 others, an rS with a notch or slur on the downward limb of S or at the peak of S was seen. In the right ventricular outflow position the R′, present in 11, increased in magnitude from the main pulmonary artery in 4, decreased in 3, remained the same in 3, abruptly disappeared in 2, and first appeared in 1. There was therefore, no correlation as to appearance, disappearance, or magnitude of the R′ from the pulmonary artery to the ventricular outflow tract.

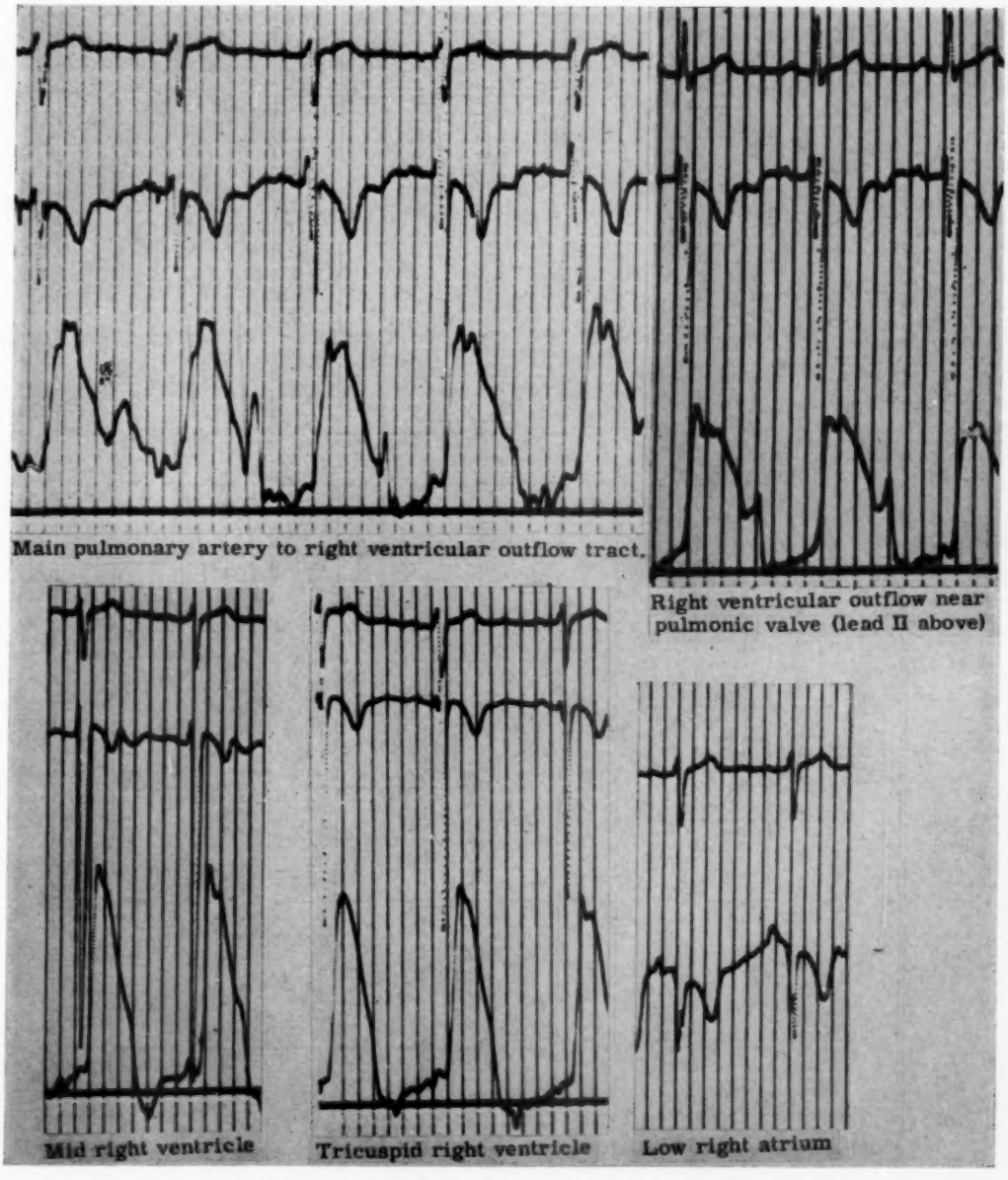


Fig. 1.—Patient J. T. Simultaneous recordings of V_{4R} (above) and endocardial lead (middle). Pressures (below). Time lines = 0.1 sec.; paper speed = 25 mm./sec.

TABLE II. SEPTAL DEFECTS

PATIENT	ENDOCARDIAL LEADS							PRECORDIAL LEADS			
	MAIN PULMONARY ARTERY	PULMONIC VALVE	RIGHT VENTRICLE			TRICUSPID VALVE	LOW RIGHT ATRIUM	V_1	V_{1R}	RIGHT VENTRICULAR PRESSURE (MM. Hg)	AGE (YR.)
			OUTFLOW	MID	TRICUSPID						
A.—Atrial Septal Defect											
W.W.	rS	rS_n	rSr′s′ .09	$r_{s1}S$	rS	RS	rS	rS	rS .09	20/2	23
E.J.	QR rSR′	0	0	rSϕ .08 r_nS	rS	rS_n	rS_n	rsr′	RS .08	30/3	54
E.H.	rSr′	rSR′S′ rsR′S′	rsR′S′ .11	r_nS	rS	rS	rS^n	rsr′	rSr′S′ .10	18/1	25
A.G.	qr^n	rsR′s′	rsR′s′ .08	rSϕ	rS	0	QR	rsr′	rsr′ .08	26/0	45
R.La.	rS_n	RsR′S′	rS .11	RS	rS	0	QS	rsr′	0	29/8	34
M.S.	rSR′s′	rSr′	rsr′S′ .11	rsr′S′ rS	rS	rS	Qr	rsR′s′	rsR′S′ .09	26/0	14
P.M.	rSR′	rsR′	rsR′ .08	rS	rS	rS_n	QR	rSr′	rsr′s′ .06	28/0	11
S.G.	rSR′	rsR′S′	RsR′S′ .10	$r_{s1}S$	rS	r_nS	r_nS	rsR′	rsR′ .08	22/3	13
C.C.	rSr′s′	0	rS .09	rS	r_nS	r_nS rsr′S′	Qrs	rSr′	rSr′ .09	18/8	25
E.C.	rSr′	rsR′S′	rsr′S′ .09	rS	rS	qr_nS	qr_nS	rR′	rsR′ .08	30/2	4½

B.R.	rS^n	rsr′S′	rSr′s′ .09	rS	$r_{sl}S$	r_nS	rSr′s′	qR .08	rsR′ .09	120/10	25
E.G.	rS^{sl} rSr′	rsR′S′	rsR′s′ .12	rsr′S′	QRS	0	qRS	qR .11	qR .10	40/2	42
J.M.	rSr′	rsR′s′	rsR′s′ .11	rS	rsr′S′	0	0	QR .10	rSR′ .11	30/8	42
E.S.	rSr′	rSR′ rSR′S′	rS .08	rS	r_nS	r_nS	0	QR .07	rSR′ .08	40/0	46
M.Br.	$r_{sl}S$	$r_{sl}S$	$r_{sl}S$ .11	rsr′S′	rS	Q_nS	Q_nS	qR .09	qR .09	96/1	26
A.M.	Rsr′S′	Rsr′S′	RSr′S′ .10	RS^n	RS^n	RSr′s′	QRS Qr	Rrs	0	28/8	4½

B.—Ventricular Septal Defect

T.H.	QR	0	rSr′S′ .08	RS	rsR′S′	rS^n	QS^n_n	RS	RS .08	55/7	20
T.Hay.	rS	RSr′	rs .09	rS	rS	rsR′	rSR′	rS	rS .09	27/1	16
T.G.	rSr′	rSr′s′	rS .08	0	rS	rsr′S′	qrS	rSr′	rSr′ .08	24/−2	13½
P.C.	rSr′ Qr	rS^n rS_n	rSr′s′ .08	rS	RS	QS_n	rSr′	RS	Rs .06	45/7	19 mo.
P.H.	rS	RSr′s′	rSR′s′ .12	Q†	Q†	0	QRS	rR′ .12	0	110/2	20
C.P.	rSr′	rS	QS .06	QS	QS qrS	QS	QRS	RS	RS .08	80/2	9
P.B.	rS	rS^n	RSr′S′ .10	rS	rS	rS	rS	RSr′S′	RSR′s′ .09	38/3	14
M.Bt.	rS	rSR′s′	rsR′S′ .09	rS	rS	QS^n	rSr′	rsR′	rsR′ .08	175/5	29

†Only initial deflection clearly seen.
sl subscript = slur on the descending limb.
Other symbols as in Table I.

Again an rS was the most common pattern seen in the mid right ventricle, the S being notched either on the descending or ascending limb in 5 patients. In 3 patients in whom an rsr′S′ persisted in this position, the r′ was equal to and smaller than the r′ of the outflow pattern. An R′ reappeared in the tricuspid area or across the tricuspid valve in 3 patients, or was reflected by notching of the S or downward r of an rS pattern in 5. A QRS was seen in 2.

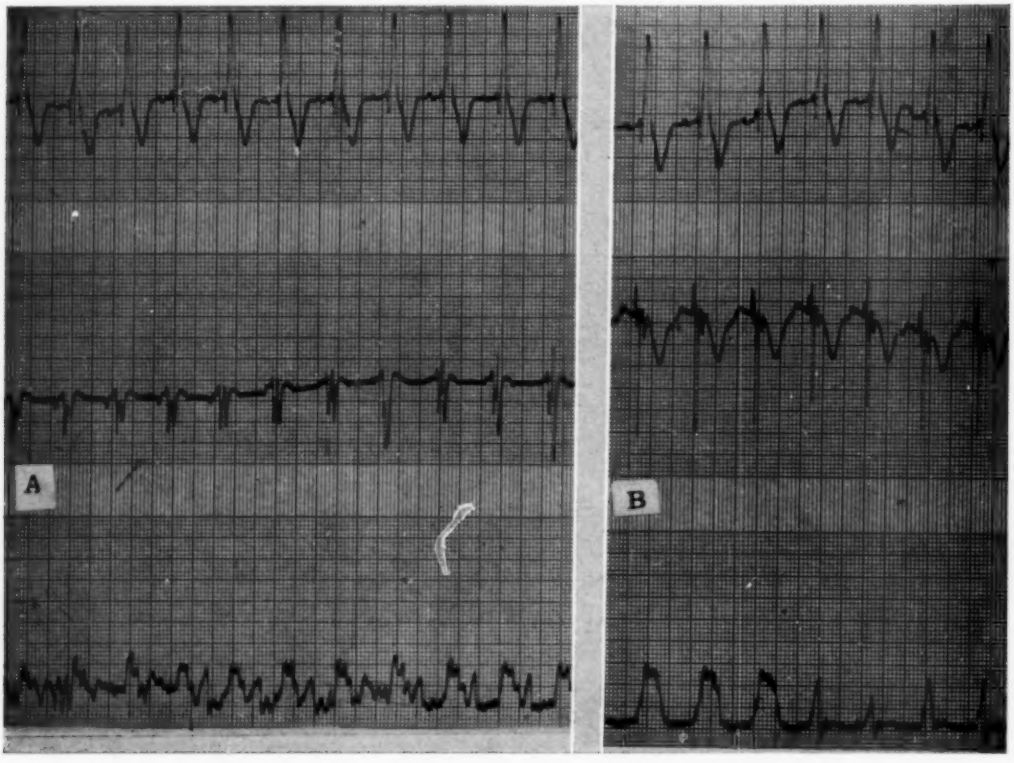


Fig. 2.—Patient D. D. Unusual patterns observed in the endocardial tracings (middle) over the pulmonic valve in *A* and over the tricuspid valve in *B*. V_{4R} above, pressure tracing below. Time lines = 0.04 sec.; paper speed = 25 mm./sec.

Group III—Ventricular Septal Defect.—The data are shown in Table II*B*. The electrocardiogram was considered within normal limits in 2 patients. Incomplete right bundle branch block was present in 2, and complete right bundle branch block in 1. Right ventricular hypertrophy and strain was diagnosed in 2, and left ventricular hypertrophy in 1.

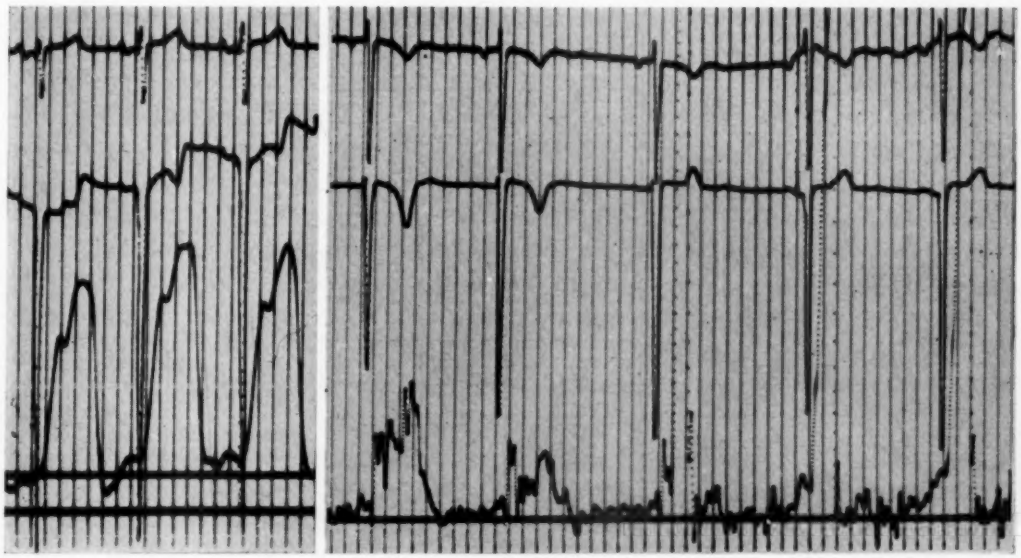
In the 7 patients in whom tracings were recorded across the pulmonic valve, an r′ was present in 5. In the right ventricular outflow position the R′ first appeared in 2 patients, increased in magnitude in 1, and was the predominant deflection in 2 with the highest right ventricular pressures.

In the patient with left ventricular hypertrophy and strain (C.P.) QS patterns were recorded in all right ventricular positions (Fig. 3,*A*).

Group IV—Cardiopulmonary Disease.—The data are shown in Table III.

The electrocardiographic diagnosis of right ventricular hypertrophy and strain was made in both patients.

In one patient, as the catheter was drawn across the pulmonic valve and into the outflow tract, the R′, previously recorded in the pulmonary artery, increased in magnitude (Fig. 4). In the other patient, an arrhythmia obscured the tracing at this time. The ventricular patterns were unusual in this patient. In the outflow and tricuspid areas an Rsr′S′ and an rsR′S′ were seen, respectively, with notching of the downward limb of S. In the mid position this notch became a



A. *B.*

Fig. 3.—Endocardial tracings (middle) showing QS complexes recorded in the right ventricle. V_{4R} above and pressure tracings below. Time lines = 0.1 sec.; paper speed = 25 mm./sec. *A*, Patient C. P.—right ventricular outflow position. Sensitivity increased to 1 mv. = 25 mm. *B*, Patient L. P.—pullback from the infundibular to the high-pressure chamber.

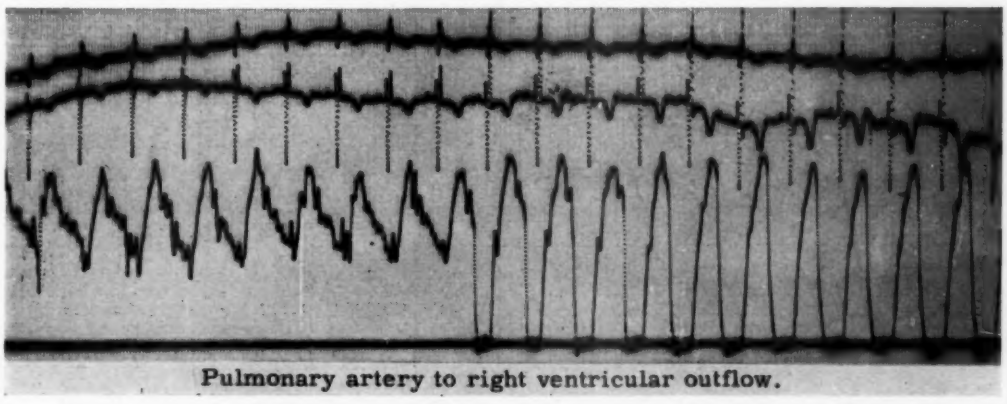


Fig. 4.—Patient A. L. with primary pulmonary hypertension. Pullback across the pulmonic valve. V_{4R} (above), endocardial lead (middle), and pressure (below). Time lines = 0.04 sec.; paper speed = 25 mm./sec.

TABLE III. CARDIOPULMONARY DISEASE

PATIENT	ENDOCARDIAL LEADS							PRECORDIAL LEADS			
	MAIN PULMONARY ARTERY	PULMONIC VALVE	RIGHT VENTRICLE			TRICUSPID VALVE	LOW RIGHT ATRIUM	V_1	V_{4R}	RIGHT VENTRICULAR PRESSURE (MM. Hg)	AGE
			OUTFLOW	MID	TRICUSPID						
T.B.	rSr′	0	Rsr′S′$_n$ .10	RSR′S′r″s″ rS	RSR′S′$_n$ rsR′S′$_n$	rsR′S′	rSr′s′ Qrs	rR′	rR′ .10	70/10	36 mo.
A.L.	rS rSr′	rSR′	rSR′ rsR′S′ .08	rS	rS	rSr′s′	rSr′s′	rsR′	rsR′ .08	64/1	2^3 yr.

Symbols as in Table I.

definite deflection and the pattern was RSR′S′r″s″, similar to that of patient D.D. shown in Fig. 2. In the low right atrium an rSr′s′ was recorded, with the r′ corresponding in time to the notch or r″ of the outflow and mid positions, respectively.

Group V—Pulmonic Stenosis.—The data are shown in Table IV*A*. In 2 patients the electrocardiogram was considered normal. Right ventricular hypertrophy and strain were present in one and complete right bundle branch block in another.

An r′ was recorded across the pulmonic valve and in the outflow tract in 2 patients. The r′ was smaller in magnitude than the initial r. In one patient (E. McN.) with elevated right ventricular pressure, an R′ was recorded in all ventricular positions and was of greatest amplitude in the mid position. In another patient (L.P.) with similarly elevated right ventricular pressure, but with pure infundibular stenosis, no R′ or r′ was recorded in the ventricle, although a QR was observed over the tricuspid valve. In the latter patient, a QS pattern was observed in the high-pressure chamber (Fig. 3,*B*), that is, in the mid right ventricle and tricuspid area, while an rS pattern was seen in the infundibular chamber. There was, likewise, a sudden change in previously inverted T waves to upright T waves in the high-pressure chamber.

Group VI—Tetralogy of Fallot.—The data are shown in Table IV*B*. The electrocardiogram was consistent with right ventricular hypertrophy and strain in all.

In 5 patients in whom endocardial tracings were recorded over the pulmonic valve, an R′ or r′ was present in all. In 1 patient (M.P.) an rsR′S′ was recorded in the aorta, with the R′ increasing in height as the catheter was withdrawn across the aortic valve into the right ventricle.

As the catheter entered the right ventricle, the r′ abruptly disappeared in 2 patients. In 2 patients in whom the infundibular chambers were entered, an rSr′S′ and RSr′S′ were seen. The r′ had increased from the main pulmonary artery position in one, and decreased in the other. In 3 with pure valvular stenosis an rsr′S′ and an rS pattern were seen in the right ventricular outflow position.

Group VII—Aortic Stenosis.—The data are shown in Table V. The electrocardiogram showed evidence of left ventricular hypertrophy and strain in 4 patients, and was considered within normal limits in 1. ST-T changes due to digitalis were present in another.

As the catheter was withdrawn across the pulmonic valve and into the right ventricular outflow tract, an R′ and R′S′ were recorded only in the 2 patients who did not have electrocardiographic evidence of left ventricular strain. In 2 patients with left ventricular hypertrophy a distinct r′ in an rsr′S′ pattern was seen only over the tricuspid valve and in the lower right atrium.

In 2 patients QS patterns were recorded in the right ventricle.

CORRELATION OF THE ENDOCARDIAL AND PRECORDIAL ELECTROCARDIOGRAM

The endocardial tracings were recorded simultaneously with V_{4R} in 36 patients and with Lead II in 14.

In 13 patients with an rS or RS in V_{4R}, an rsR′S′, RSr′S′ or rSr′ was recorded

TABLE IV. PULMONIC STENOSIS

PATIENT	ENDOCARDIAL LEADS							PRECORDIAL LEADS			
	MAIN PULMONARY ARTERY	PULMONIC VALVE	RIGHT VENTRICLE			TRICUSPID VALVE	LOW RIGHT ATRIUM	V_1	V_{4R}	RIGHT VENTRICULAR PRESSURE (MM. Hg)	AGE (YR.)
			OUTFLOW	MID	TRICUSPID						
A.—Pure Pulmonic Stenosis											
J.H.	rSR′	rsr′s′	rsr′S′ .08	rS	rS	rSr′s′	rSr′s′	rS	rS .08	82/4	23
L.P.	QS	rS	rS§ .08	QSφ .07	QS	QR	Qr	rS	RS .08	12/1§82/3	39
R.L.	rS r_nS	r_nS	rS .08	0	0	0	0	R	qR .07	52/0	21
E.McN.	rS*1	Rsr′S′	RSr′S′ .12	RSR′S′	r_nS	rsr′S′	rsR′	rsR′	rsR′ .12	94/0	28
B.—Tetralogy of Fallot											
J.E.	rSr′s′	rSr′S′	rS .08	rS	rS	r^nS	r_nS	rR′	rsR′ .08	98/3	2
J.S.	RSr′	RSR′S′ Rsr′S′	rS .10	rS	0	0	0	rsR′	rsR′ .10	76/0	6
C.McC.	rS	rSr′	Rsr′S′§ .08	RS	rS	rS_n	QS	rR′	rR′ .08	40/0§80/0	9½
J.C.	rSR′ rS	rSR′	rS rSR′§	rS	rS	0	QR	rR′	0	24/10§110/0	22
M.P.	rsR′s′‡	0	0	rS	rsR′	rsR′	rsR′	R	0	118/78	28
C.S.	rR′	rR′	rS .10 rsr′S′	rS	0	0	0	R	R .10	152/12	17

‡Aorta.
§Infundibular chamber.
Other symbols as in Tables I and II.

§Infundibular chamber.
Other symbols as in Tables I and II.

TABLE V. AORTIC STENOSIS

PATIENT	ENDOCARDIAL LEADS							PRECORDIAL LEADS				
	MAIN PULMONARY ARTERY	PULMONIC VALVE	RIGHT VENTRICLE			TRICUSPID VALVE	LOW RIGHT ATRIUM	V_1	V_6	RIGHT VENTRICULAR PRESSURE (MM. Hg)	AORTIC SYSTOLIC GRADIENT (MM. Hg)	AGE (YR.)
			OUTFLOW	MID	TRICUSPID							
H.W.	rS	rS	rS	RS	0	rsr′S′	QS	rs	$R_{s\text{-}t,t}\downarrow$	38/7	124	38
E.McC.	Q_nS	QS	QS	QS	QS	$Q_{s1}S$	0	QS	$R_{s\text{-}t,t}\downarrow$	24/3	25	58
E.E.	rS	rS	rS	QS	QS	QS	$Q_{s1}S$	QS	$R_{s\text{-}t,t}\downarrow$	16/0	—	58
P.E.	rS	0	0	RS	rS	QS Qr	rS rSr′	rS	$qR_t\downarrow$	20/0	36	35
W.B.	rS^n	rSR′	rsR′	rS_n	0	0	rS	rS	$R_{s\text{-}t,t}\downarrow$	28/3	68	52
J.J.	rSr′	RSR′s′	RSR′S′	rS	rS	rSr′	rS^n rSr′	rS	qR	20/3	13	56

$\downarrow$ = s-t depression and t-wave inversion.
Other symbols as in previous tables.

over the pulmonic valve or in the right ventricular outflow tract in 11. In general, the endocardial complex began simultaneously with or up to 0.03 second before the peripheral lead. The QRS duration was similar to or slightly longer than that of V_{4R}. The endocardial R′ or r′ occurred simultaneously with the peripheral S or with a notch just after the peak and on the ascending limb of S (Fig. 5, *A* and *B*). The endocardial S′ occurred on the ascending S of V_{4R}.

In 6 patients with an rsr′, and in 14 with an rsR′ in V_{4R}, ranging in duration from 0.06 to 0.12 second, the endocardial R′ of the ventricular outflow and/or tricuspid positions generally occurred simultaneously with the r′ of R′ of V_{4R} (Fig. 6*A*). The endocardial S′ occurred slightly after the peak and on the downward R′. In some cases the endocardial R′ occurred slightly before and, in one case, slightly after the peak of R′ in V_{4R}. The R′S′ was recorded almost instantaneously in many.

In 4 patients with a qR in V_{4R}, the endocardial complex was 0.01 to 0.02 second longer in duration and began 0.01 to 0.03 second earlier in all. Initial r waves were present in the right ventricle in all of these patients. In 2 patients in whom an R′ or r′ was recorded over the pulmonic valve, tricuspid valve or in the right ventricular outflow tract, the endocardial R′ occurred simultaneously with the late R of V_{4R} and the S′ occurred on the downward limb of the late R (Fig. 6*B*). An rS with slurring of the downward S was recorded by the endocardial lead in the other 2 patients.

In 3 patients a qR in V_1 became an rsR′ in V_{4R}. An initial r was present in all right ventricular positions, and an R′S′ or r′s′ was recorded over the pulmonic valve or in the right ventricular outflow tract in all.

In 1 patient (C.S.) with a single large R in V_1 and V_{4R}, the endocardial R′ occurred simultaneously with the peripheral R, and the endocardial S′ occurred on the downward limb of R (Fig. 6*B*).

In those patients in whom Lead II was recorded simultaneously with the endocardial lead, the intracavitary R′ occurred simultaneously with the descending limb of R or S in 4 patients, with the peak of S in 6 patients, and at the end of R in 1 patient, with varying patterns in Lead II—qR, qRs, RS, RSr′. The endocardial S′ occurred with the peak or on the ascending limb of S (Fig. 5, *C* and *D*).

In 2 patients, complex patterns were observed in the right ventricle, consisting of RSr′s′r″s″. By a comparison of the duration of each deflection with simultaneously recorded V_{4R} and Lead II, it was found that the r″s″ corresponded, respectively, to the R′ and downward limb of R′ in V_{4R} (Fig. 2) and to the S of Lead II, and therefore to the usual endocardial R′S′ observed in other patients. These complexes were constant and did not appear to be due to artifact. An explanation for the intermediate r′s′ is difficult to propose at this time.

CORRELATION OF THE ENDOCARDIAL LEADS WITH CLINICAL AND PHYSIOLOGIC DATA

Examination of the endocardial patterns with respect to age of the patient, type of lesion, and right ventricular pressure failed to reveal exact correlations. The height of the R′ in relation to the initial r was used rather than the absolute magnitude of R′.

The R′ was predominant in the right ventricular outflow position in 1 of 13 patients under the age of 13 years, and in 7 of 15 patients over the age of 25 years, and excluding those with left ventricular hypertrophy.

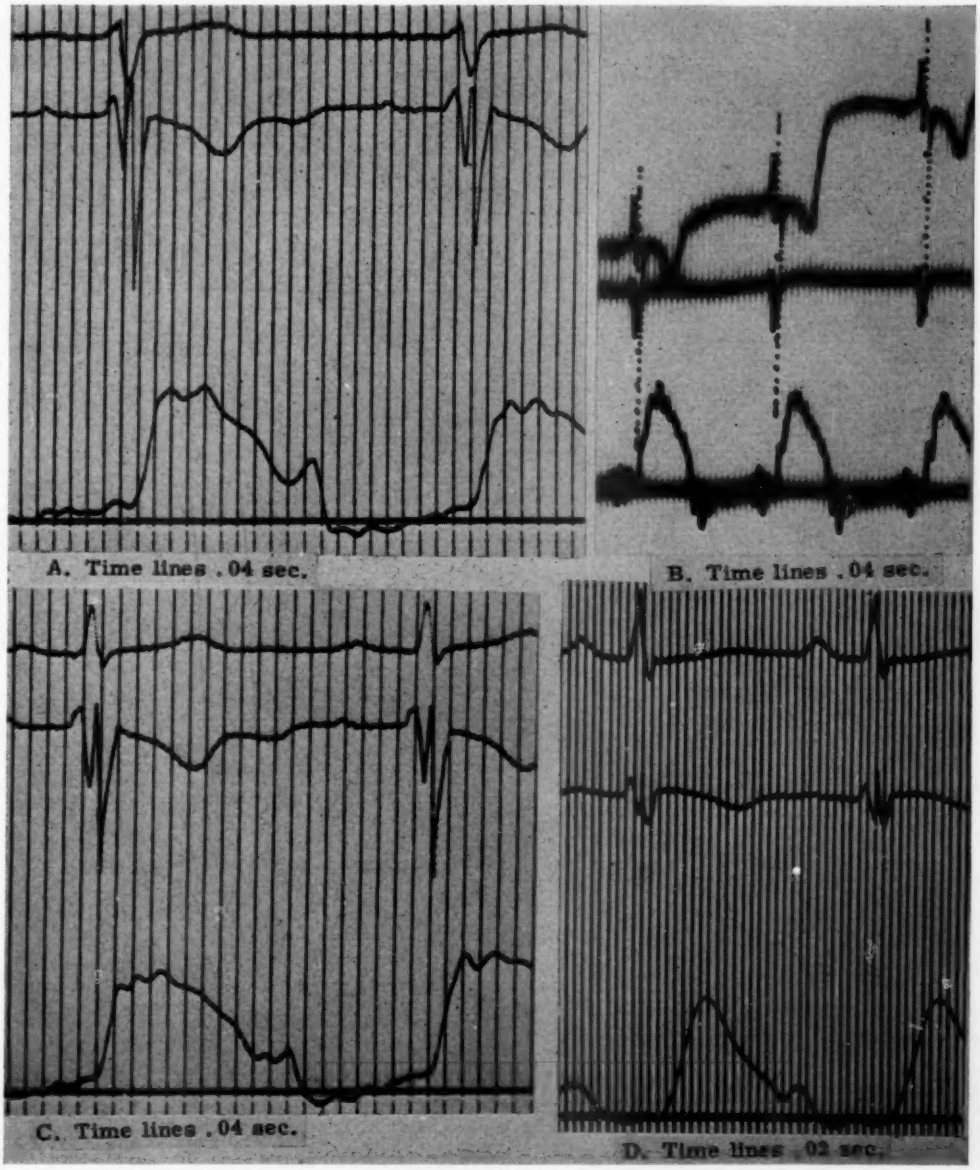


Fig. 5.—Correlation of the endocardial tracings with an rS pattern in V_{4R} (*A* and *B*) and with an Rs pattern in Lead II (*C* and *D*). Paper speed of tracings *A*, *C*, and *D* = 75 mm./ sec., and of *B* = 25 mm./sec.

A predominant R′ over the pulmonic valve or in the right ventricular outflow tract was seen in 6 of 14 patients with an rS or RS in V_1, excluding 5 patients with left ventricular hypertrophy, in 4 of 8 patients with an rsr′, in 7 of 13 patients with an rsR′, in 3 of 6 patients with a qR, and in 2 of 3 patients with an R in

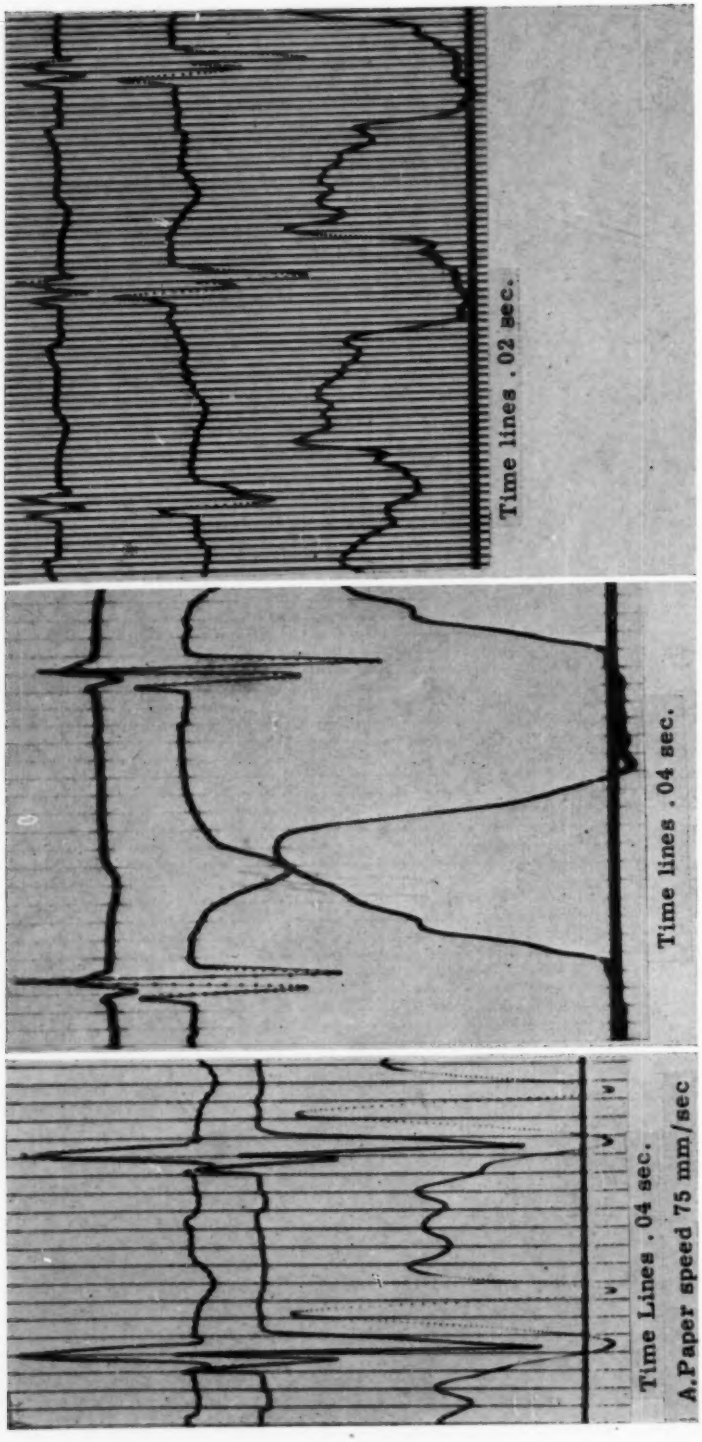


Fig. 6.*A*.

Fig. 6.—*A* and *B*, Correlation of the endocardial lead (middle) recorded in the right ventricular outflow tract with varying V_{4R} precordial patterns (above).

V_1. No absolute relationship was seen between the height of the R′ in the endocardial lead and the height of R or R′ in V_1 or V_{4R}. This probably reflects the effect of position of the precordial lead with relation to the heart and septal activation, as well as of some movement of the intracavitary lead. Inability to maintain the catheter directly on the endocardial surface may also explain the unexpected and varying changes in the height of the R′ from the pulmonary artery to the outflow tract of the right ventricle. There was likewise little relationship between the height of the endocardial R′ and duration of QRS in V_{4R}.

There was no correlation between the endocardial R′ and the type of cardiac lesion, or the right ventricular pressure. In the total group, a predominant R′ was seen over the pulmonic valve or in the right ventricular outflow tract in 13 of 23 patients with elevated right ventricular systolic pressure. In 25 patients with normal pressures, a predominant R′ was seen in 12 over the pulmonic valve and in 8 in the right ventricular outflow position.

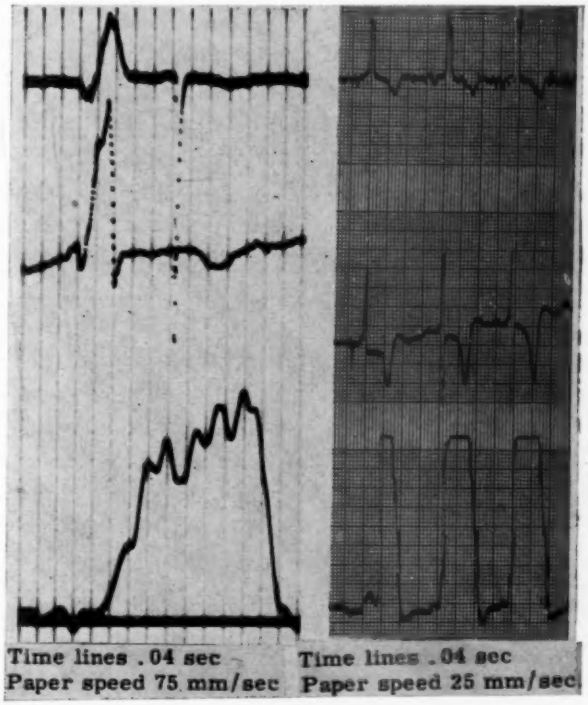


Fig. 6,*B*.—(*For legend see opposite page.*)

COMMENT

The interpretation of the V_1 pattern has been the subject of much discussion and disagreement. The RSR′ in V_1 has been variously ascribed to right bundle branch block,[2,5] right ventricular hypertrophy,[6-8] and no abnormality.[9,10] The origin of the R′ in this pattern has likewise had numerous interpretations. Some investigators, utilizing endocardial leads, have suggested a dual origin due to depolarization of the septum and free right ventricular wall,[11] or to late anomalous

activation of the right septal mass followed by activation of the free right ventricular wall in right bundle branch block.[12] Others attributed the R′ deflection to activation of the crista supraventricularis[13,14] or to the normal or hypertrophied pulmonary conus.[10,15,16]

In the present study it has been observed that the endocardial R′ over the pulmonic valve or right ventricular outflow tract occurs synchronously with the R′ of an rSR′ in V_{4R}, with the late R of a qR in V_{4R}, and with the S of an RS in Lead II. This suggests that the direction of activation during inscription of the R′ is upward and to the right, toward both the intracavitary and precordial leads. It may be directed anteriorly (rsR′ in V_1) or posteriorly (rS in V_1). The endocardial S′ occurs slightly afterward and on the downward R′ or late R of V_{4R}, indicating that at this time the activation wave, while still approaching the peripheral lead, is away from the endocardial lead. Were the peripheral late R or R′ to originate in the free right ventricular wall,[8,16,17] an entirely negative deflection would occur in the intracavitary lead simultaneously with a positive deflection in the peripheral lead. The inscription of first a positive (R′) then a negative (S′) endocardial deflection simultaneously with a peripheral positive deflection can occur if the force originates in the upper septum. It has been shown experimentally in dogs[18] by means of bipolar transeptal leads that the initial activation of the septum occurs in the lower one third close to the anterior papillary muscle. The present study supports the concept of early activation of the lower septum from left to right, followed by activation of the left and right free ventricular walls, and later activation of the upper septum followed finally by the free right ventricular wall below the pulmonic and tricuspid valves. This mode of activation is reflected by the recording of an rSR′S′ in the right ventricular outflow tract, an rS in the mid right ventricle, and recurrence of the RSR′S′ pattern in the tricuspid area as the catheter again approaches the upper septal area. The R′ was generally of greater prominence in the outflow tract, probably because of closer contact of the catheter with the upper septum than in the tricuspid area. An S′ was usually recorded in the outflow tract and less commonly in the tricuspid area, and is attributed to final activation of the free right ventricular wall in a direction away from the endocardial lead.

That the RSR′S′ recorded in the right ventricle is not due solely to right bundle branch block with anomalous activation of the septum, as suggested by Sodi-Pallares and associates,[5,12] or solely to hypertrophy of the right ventricle,[16] is shown by the finding in this study of similar patterns in the right ventricle of normal individuals with normal electrocardiograms, and of patients with a variety of cardiac lesions and with routine electrocardiograms which are normal or show criteria for right ventricular hypertrophy[1] or right bundle branch block.[2,3] It is of interest that vectorcardiographic evidence for either right ventricular hypertrophy or right bundle branch block can be demonstrated in the presence of an rSR′ complex in V_1.[17] It is apparent, then, that the pattern of activation of the heart is not altered in right bundle branch block or right ventricular hypertrophy from the normal, and morphology alone cannot be used to differentiate the two. It is also suggested that later activation of the upper septum, repre-

sented by the R′ of endocardial leads, occurs normally as well as in right ventricular hypertrophy or right bundle branch block. Late anomalous activation of the lower septum may be reflected by the occurrence of an R′ in all ventricular positions in cases of complete right bundle branch block. Endocardial studies, therefore, do not support the concept that right ventricular free wall hypertrophy alone produces a prominent R or R′ in V_1, as suggested by some observers,[16] since the latter deflections may reflect mainly the upper septum. The free wall is generally represented only in the latter portions of the peripheral R or R′, which occur simultaneously with the endocardial S′.

That similar ventricular endocardial complexes may be found with a variety of V_1 precordial patterns (rsr′, rsR, qR,R, rS) remains to be explained. It was likewise observed that there was little relation between the endocardial R′ and the height of the peripheral R, r, or late R. It is apparent that by proximity the endocardial lead records the R′ of upper septal activation, while the peripheral lead is affected by numerous factors, such as the distal effects of right and left ventricular activation, position of the heart with relation to the precordial lead, and the relative predominance of the left ventricle. The effect of the latter, particularly when a precordial rS does not reflect an endocardial rsR′, may be seen in normal persons and in patients with electrocardiographic evidence of left ventricular hypertrophy. The endocardial r′ was smaller than the initial r in the majority of patients with normal electrocardiograms. In patients with left ventricular hypertrophy on the routine electrocardiogram, an r′ was not recorded in the right ventricular cavity in any. The intracavitary S deflections, reflecting left and right ventricular depolarization, were of great depth, probably obscuring the r′ usually recorded near the upper septum.

The effect of the position of the heart with respect to the precordial lead may be of even greater importance in determining the morphology, as well as the magnitude, of the V_1 or V_{4R} pattern. This may be seen by examination of the tracings presenting a qR in V_1. An initial r was observed in the right ventricle in all. The duration of the endocardial complex was similar to the rsR′ of V_{4R}, and greater than the qR of V_1. Other investigators have attributed the qR pattern in V_1 to a variety of causes. Wilson and associates[20] proposed a theory of decreased density of the junction of Purkinje fibers and ordinary heart muscle in certain areas due to chamber dilatation. Kossmann and associates,[21] Goldberger,[15] and McGregor,[22] using epicardial leads, attributed the q to the posterobasal portion of the left ventricle with extreme clockwise rotation of the heart. Theories of abnormal septal activation were also proposed by Myers,[23] and Fowler.[17] Marsico and co-workers,[24] on the basis of one case, concluded that reversed septal activation occurred because of predominance of the right septal mass, while Kert and Hoobler[11] suggested that the left ventricle was rapidly activated before the septum. Despite these numerous theories, it can only be concluded from the above studies that the initial r of a qR pattern in V_1 or V_{4R} is isoelectric due to position of the electrode with regard to early initial septal activation. Furthermore, it can be demonstrated that the endocardial R′ is simultaneous with the late R of a qR in V_{4R} when an initial isoelectric r is taken into consideration.

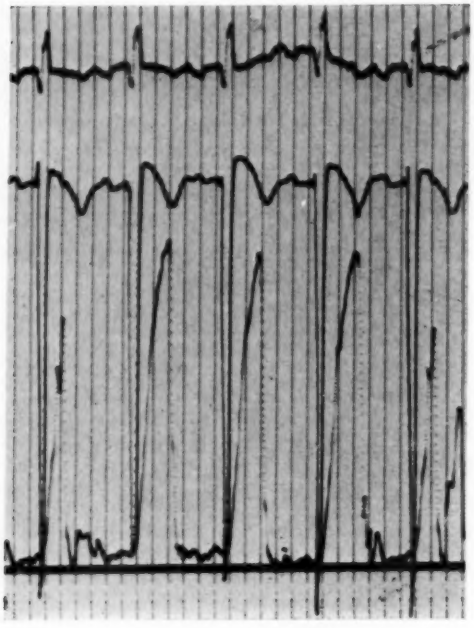


Fig. 7.—Continuous tracing recorded in the mid right ventricle, showing the effect of changing catheter position with respect to initial septal activation. The duration of QS complexes is less than the rS patterns. V_{4R} (above), endocardial (middle). Time lines = 0.1 sec.

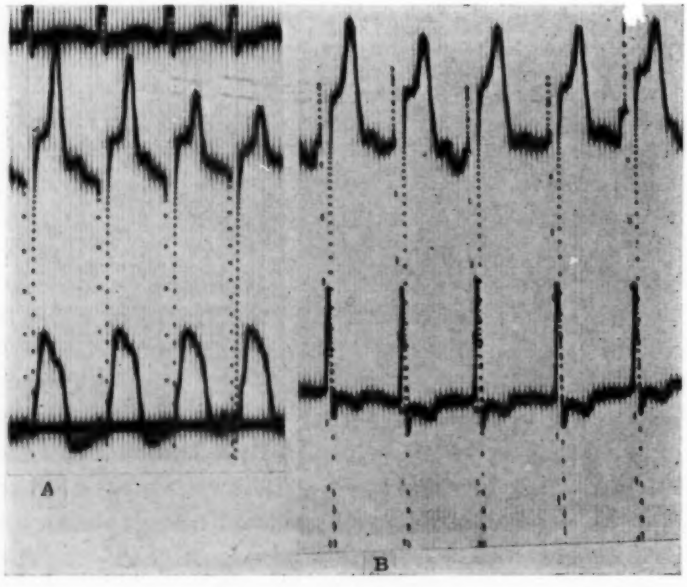


Fig. 8.—Patient E. E. with aortic stenosis. Endocardial tracings (middle) obtained in the right ventricle (*A*) with Lead II (above), and in the left ventricle (*B*), with V_6 (below). Note the initial Q and the initial R in the right and left ventricles, respectively. Time lines = 0.04 sec.; paper speed = 25 mm./sec.

Besides the effects of cardiac position and left ventricular predominance upon the variability of the precordial pattern, other factors may be considered when dealing with patients with congenital lesions affecting primarily the right ventricle. It is possible that right upper septal and free wall activation may be reflected in an rSR′ pattern in V_1 and/or V_{4R} if delay of septal activation and/or hypertrophy of these areas permits their excitation to occur unopposed by the normally predominant left ventricular activation.

A final comment can be made concerning the recording of initial q waves in the right ventricle. In some cases this may result from varying catheter position. Continuous recording in the mid right ventricle in an occasional patient (Fig. 7) resulted in a series of complexes with and without an initial r deflection. Vigorous rapid movements of the catheter were noted. It is suggested that the variations are due to change in position of the catheter in regard to the septum. It is of interest in this respect that Prinzmetal and associates,[25] studying conduction in normal dogs, recorded initial r waves only close to the septum.

The recording of QS deflections in the right ventricle in patients with electrocardiographic evidence for left ventricular hypertrophy, on the other hand, must be qualified. In one of these patients in whom left ventricular and right ventricular endocardial leads were recorded[26] (Fig. 8) an rS pattern was observed in the left ventricle, suggesting left bundle branch block with reversed septal activation.[5]

SUMMARY

1. Fifty patients were studied by simultaneous right ventricular endocardial and precordial leads, including 8 normal patients, 6 patients with pure aortic stenosis, and 36 patients with congenital heart lesions affecting chiefly the right ventricle.

2. In general, a consistent group of patterns is observed in the right ventricle as the catheter is positioned in each area from the pulmonary artery to the low right atrium.

3. It is shown how the activation of the heart is reflected in the endocardial tracings in different ventricular positions.

4. By comparison of simultaneous endocardial and precordial tracings, it is concluded that the R′ of both leads may be attributed to upper septal activation.

5. Similar endocardial patterns are obtained in normal subjects and in patients with congenital cardiac lesions, as well as in patients with normal electrocardiograms and in those with electrocardiographic criteria for right ventricular hypertrophy or right bundle branch block. The mode of activation of the heart is not altered from the normal in these two conditions. An r′ was not recorded in the right ventricle of patients with electrocardiographic evidence for left ventricular hypertrophy.

6. The variation in the precordial patterns with similar endocardial patterns is a reflection of the influence of cardiac position and the distal effects of left ventricular predominance on the precordial lead.

7. Exact correlations between the endocardial patterns with respect to age, type of lesion, right ventricular pressure, and type of peripheral electrocardiogram could not be made.

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A Criterion Characterizing the Orientation of a Vectorcardiogram in Space

H. C. Burger, D.Sc., and J. P. Vaane, M.S., Utrecht, Netherlands

In describing and discussing the vectorcardiogram (VCG) there are numerous aspects which merit mention. As it is impossible to consider them all, a selective restriction is mandatory. Among them the concept of the ventricular gradient, which has the direction of the mean heart vector, is now well known. In the case of an elongated loop it nearly coincides with its long axis. In many cases this vague definition has to be replaced by a more exact one, in a way that will not be explained here.

Another criterion of a VCG, often used by different investigators, is the sense of rotation in its projections. The majority of QRS loops of normal vectorcardiograms have a clockwise frontal projection and a counterclockwise horizontal one. If a projection of a VCG has a more or less circular shape, it is easy to determine its sense of rotation. However, if it is very narrow, it often has a figure-of-eight shape and an ambiguous direction of rotation. But in space it may be a widely opened loop, which by its position in space is projected as a narrow one, or even as a single line. This is the case if the loop lies in a plane perpendicular to the plane of projection. The position of the plane of the loop in space has been discussed by several investigators.[1-3] In a recent article, W. R. Milnor[4] gave a criterion characterizing the position of the QRS plane in space. Using similar reasoning, we have developed a method which is based on the following:

Two projections of a loop, together with their sense of rotation, determine the loop in space with its sense of rotation. The position of the plane of the loop in space, as well as its sense of rotation, can be indicated by one single vector; for example, when the loop lies in a plane, it is a vector perpendicular to this plane and drawn at the side, in which the rotation seen is counterclockwise. Its length indicates the area of the loop and must, therefore, be chosen proportional to it. Its origin may be taken arbitrarily. This vector we will call the polar vector. It may be well to note that this is not the heart vector.

In general, however, the loop does not lie in a plane. Then the definition of the above-mentioned vector can be generalized in such a way that its rectangular components are proportional to the areas of the projections of the loop on the three coordinate planes, an assertion which we shall prove.

From the Department of Medical Physics, Physical Laboratory of the University of Utrecht, Utrecht, Netherlands.

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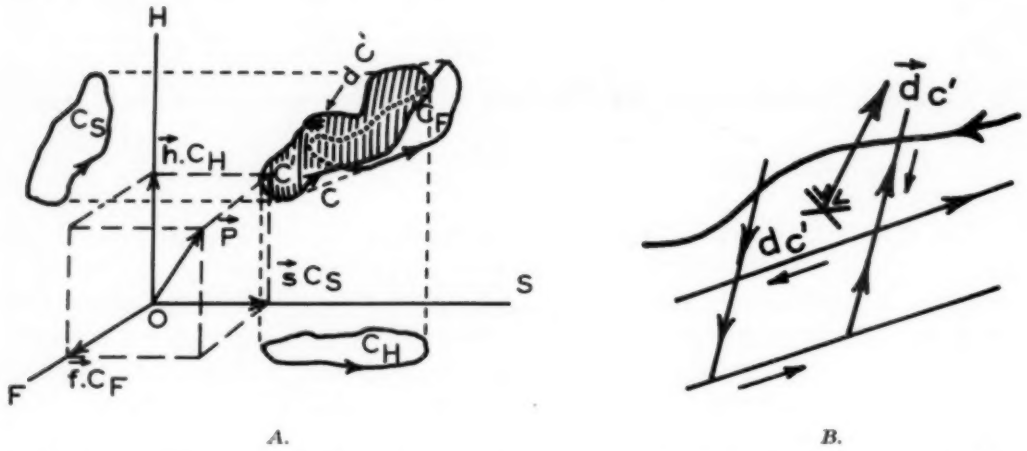
Let C (Fig. 1,*A*) be an abritrary closed curve in space. C′ is a curved surface circumscribed by C. The three mutually perpendicular axes F, H, and S are drawn so that the H axis is the head-to-foot direction of the patient, the F axis is perpendicular to the frontal plane of the patient, and S is the sagittal axis.



A. *B.*

Fig. 1.—*A*, The polar vector in relation to an arbitrary QRS loop and its projections. *B*, An infinitesimal surface, dC′, part of the surface C′ through the QRS loop, and the accessory infinitesimal polar vector $\vec{dC}'$.

We call the area of the projections of C on the FS, HS, and FH planes, respectively, C_H, C_F, and C_S; $\vec{h}$, $\vec{f}$, and $\vec{s}$ are unit vectors along the positive H, F, and S axes. Now we define as the polar vector, $\vec{P}$ of C, the vector

$$\vec{P} = \vec{h} \cdot C_H + \vec{f} \cdot C_F + \vec{s} \cdot C_S.$$

This vector is by definition independent of the shape of C′, and perfectly fixed by C because the projections C_H, C_F, and C_S are so.

Next, we define still another vector, $\vec{P}'$. Herein we divide C′ into infinitesimal surfaces, dC′, the contours of which run in the same sense as the QRS-loop C (Fig. 1,*B*). To every surface dC′ we define an infinitesimal vector, $\vec{dC}'$, with a direction and length corresponding in the same way to the sense of rotation and area of dC′, if the loop lies in a plane, as the polar vector $\vec{P}$ would correspond to C. By integration over the surface C′ we define:

$$\vec{P}' = \int_{C'} \vec{dC}'$$

and $\vec{P}'$ is fixed by the shape of C′.

Now, if we prove that $\vec{P} = \vec{P}'$ for every arbitrary surface circumscribed by C, the truth of our theorem, "the rectangular components of the polar vector are proportional to the areas of the projections of the QRS loop on the coordinate planes," is established.

Let C again be a closed curve in space, and C′ a curved surface circumscribed by C (Fig. 2). We require that C and C′ are a curve and a surface, which can be differentiated and integrated, and which are, therefore, continuous. Once more we divide C′ into infinitesimally small surfaces, dC′, with the corresponding vectors $\vec{dC}'$ having a length proportional to the area of dC′. Looking at

the projection C_F of C′ it may be readily seen that for every surface dC′ lying at the "front" of C′ a surface dC'_1 corresponds at the "back" of C′, with exactly the same projection on the HS plane, except for the dC'_1's with their projection lying at or within C_F. Because the corresponding dC″s and dC'_1's have opposite signs, C_F fixes the projection of C′ on the HS plane. If C′ is so shaped that the projection of a part of its "front" falls within C_F, there must be another part, its "back," with the same projection and opposite sign, because of the fact that the curve and the surface are continuous. Therefore, in that case, C_F will also be "the" projection of C′ on the HS plane.

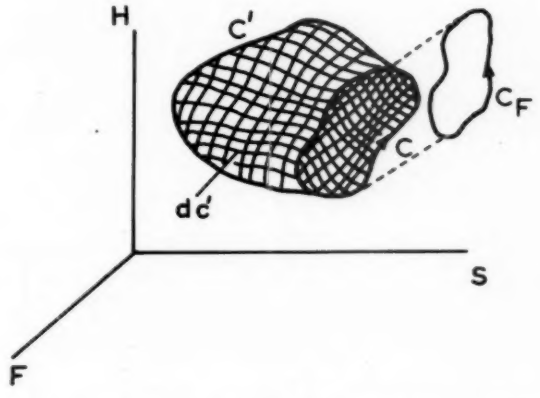


Fig. 2.—An arbitrary surface circumscribed by a QRS loop.

In the same way we prove that C_S and C_H are "the" projections on the FH and SF planes, respectively. Now let dC'_S, dC'_F, and dC'_H be the projections of dC′ on the FH, SH, and SF planes, respectively; then the vector $\overrightarrow{dC'}$ is fixed by the equation:

$$\overrightarrow{dC'} = \vec{h} \cdot dC'_H + \vec{f} \cdot dC'_F + \vec{s} \cdot dC'_S.$$

The polar vector $\vec{P}'$ of C is the integral of the $\overrightarrow{dC}$ ″s over C′:

$$\vec{P}' = \int_{C'} \overrightarrow{dC}' = \vec{h} \cdot \int_{C'_H} dC'_H + \vec{f} \cdot \int_{C'_F} dC'_F + \vec{s} \cdot \int_{C'_S} dC'_S$$

The three integrals are apparently the areas of C_H, C_F, and C_S, respectively.

Thus the following equation holds:

$$\vec{P}' = \vec{h} \cdot C_H + \vec{f} \cdot C_F + \vec{s} \cdot C_S$$

and the right side is the vector, with the components being the projections of the curve C on the coordinate planes. Therefore, we have proved the aforementioned theorem: "The rectangular components of the polar vector are proportional to the areas of the projections of the QRS loop on the coordinate planes."

The evaluation of the vector $\vec{P}$ is easy if the three rectangular projections of the QRS loop of a vectorcardiogram are recorded. Their areas give the three components of the previously mentioned polar vector.

In order to obtain the three rectangular projections of the QRS loop, we connected a patient to a vectorcardiograph. The essential property of this apparatus is that the leads (the voltages measured between the electrodes when connected to the patient) are amplified, attenuated, and combined by sets of

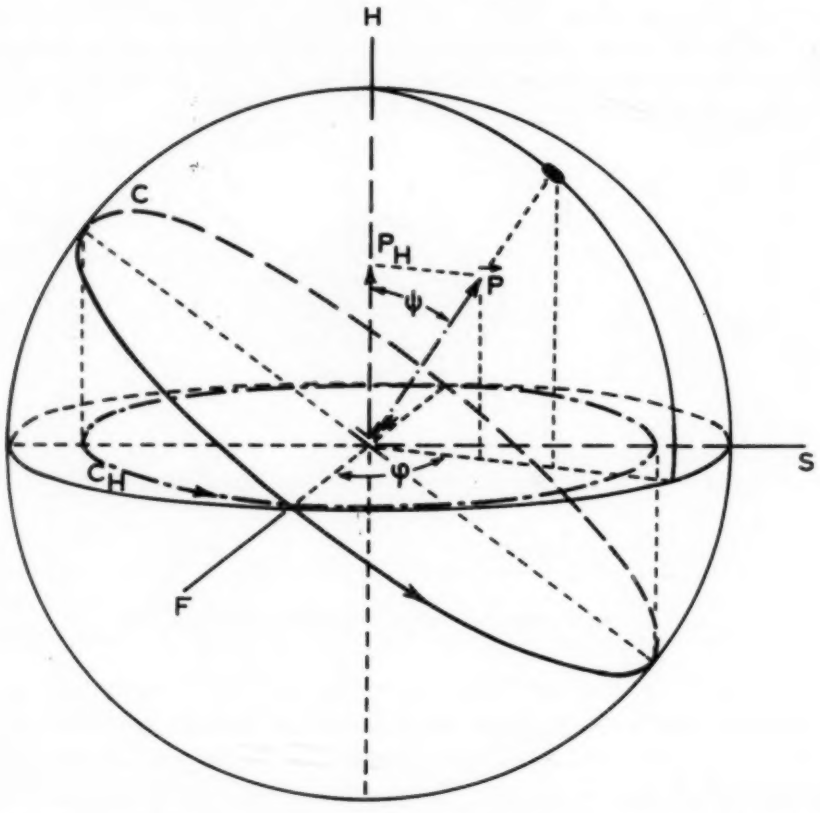


Fig. 3.—The method used to determine the coordinates φ and Ψ of the polar vector from the projections of the QRS loop.

resistances, so that finally the three perpendicular projections of the vectorcardiogram appear successively on the screen of a cathode-ray tube by selecting the appropriate position of a switch. The lead system we used is the B_1 system, which we published years ago. In this system the electrodes are fixed on the left and the right upper arm, on the sternum at the height of the axilla, and on the right leg. In Fig. 3 a QRS-loop C is drawn, situated arbitrarily in space. In the same picture the three mutually perpendicular axes F, H, and S are drawn. Only one projection of the loop C, the horizontal one, C_H, is drawn, in order to keep the picture as clear as possible.

Now let $\vec{P}$ be the polar vector, its length being proportional to the area of C. Because of the vector character of $\vec{P}$, P_H being its component along the H axis, the length of P_H is proportional to the area of C_H. In a similar way the length of the other two components of $\vec{P}$, P_F and P_S, indicate the areas of the projections C_F and C_S, respectively.

The projections C_H, C_F, and C_S now appear at will on the screen of the cathode-ray tube. Thus, by making a picture of the screen we obtain the length of the components P_H, P_F, and P_S from which the angles φ and Ψ, determining the direction of $\vec{P}$, can be computed (Fig. 3).

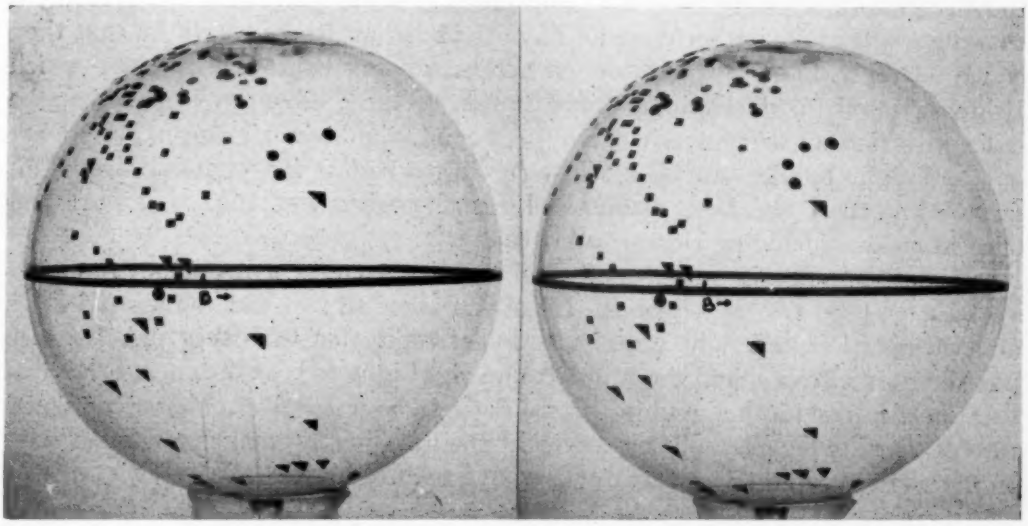


Fig. 4*A*.—Stereoscopic picture of the globe. ■ = Normal cases (100). ● = Left ventricular hypertrophy (23). ◥ = Right ventricular hypertrophy (19). The letter B indicates the back (180°) of the patient.

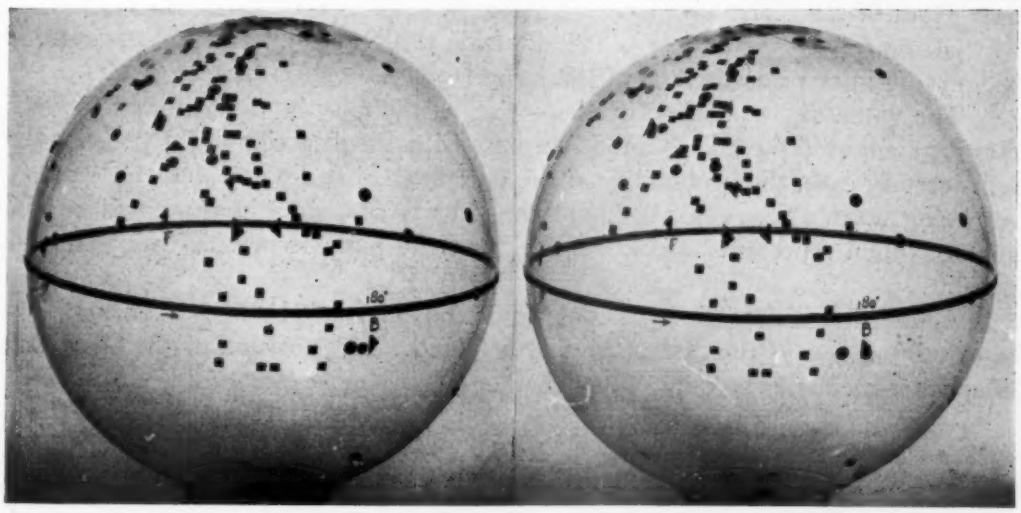


Fig. 4*B*.—Stereoscopic picture of the globe. ■ = Normal cases (104). ◀ = Left bundle branch block (7). ▶ = Right bundle branch block (13). ▲ = Other disturbances in conduction (5). ● = Infarcts (22). The letters B and F indicate, respectively, the back (180°) and the front (0°) of the patient.

Since the polar vector is drawn at that side of the loop C from which its sense of rotation is seen counterclockwise, the signs of the components of $\vec{P}$ are fixed by the direction of the polar vector and are obtained in the same way as the direction of $\vec{P}$ is obtained from the sense of rotation of C.

By the method described above we took vectorcardiograms from some 200 subjects, some with pathologic heart conditions, the rest normal, and calculated the direction (φ, Ψ in Fig. 3) of the polar vector. We did not take into consideration the *length* of $\vec{P}$, but let them all have the same arbitrary length, so that they could be represented by points on a sphere, analogous to the method which Brinberg[7] used for determining the situation of the gradient. We divided the cases into normal, left ventricular hypertrophy, right ventricular hypertrophy, left and right bundle branch block, other disturbances in conduction, and infarct. The cases had been diagnosed by cardiologists who employed the usual clinical means, including electrocardiography.

In order to obtain a clear picture of the directional distribution of the polar vectors, we used two glass globes. On one of these (*A*) we put the normal cases and those of left and right ventricular hypertrophy; on the other globe (*B*) we put the normal cases, and those of left and right bundle branch block, other disturbances in conduction, and infarcts. Figs. 4*A* and 4*B* give a stereoscopic picture of these two globes. They represent the data just as well as a list of values of the angles φ and Ψ, which we will not reproduce here.

CONCLUSION

Seventy-five per cent of the normal cases lie in the octant given by $90° < \varphi < 180°$, $\Psi < 90°$.

Sixty-three per cent of the right ventricular hypertrophies lie below the equator, having φ near 180° (back); the left ventricular hypertrophies lie on the upper half of the globe with φ near 0° (front).

Of the other cases 80 per cent lie outside the "normal" area, 50 per cent of them lying in or near the area of left hypertrophy.

The value of the method in diagnosing a case may be described as follows: Having computed the angles φ and Ψ representing the direction of the polar vector for a certain case, the probability of the patient having a particular abnormality (or being normal) is proportional to the density of points in the cloud on the sphere, which represents this abnormality at the point found for the particular patient.

As in other diagnostic methods, the final diagnosis is better established only after more facets of the disease are investigated. The position of the QRS loop in space is meant to be only one of them.

SUMMARY

The orientation of the plane of the QRS loop of a vectorcardiogram can be described by its polar vector. In a number of cases (normal as well as abnormal) the direction of this vector has been determined and displayed on a globe. The distribution of points on this globe may be of help in diagnosing the abnormality from the vectorcardiogram.

We wish to express our thanks to J. B. van Milaan, Ph.D., and A. G. W. van Brummelen, M.S., for their help with the development of the method, and to H. Schneider, B.S., for collecting a great part of the data.

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Myocardial Infarction in the Wolff-Parkinson-White Syndrome: A Method of Vector Analysis of ECG Changes

William D. Angle, M.D., Omaha, Neb.

This paper presents a method of vector analysis of the ventricular depolarization complex in serial electrocardiograms, permitting recognition of myocardial infarction in the presence of anomalous atrioventricular excitation, the Wolff-Parkinson-White (WPW) syndrome.

Twenty-two cases of myocardial infarction in the presence of the WPW syndrome have been reported.[1-13] Electrocardiograms were published in 16 of these cases. Electrocardiograms during normal atrioventricular excitation were published in 10 cases, and in 2 cases these electrocardiograms showed a normal QRS, while in the other 8 cases QRS changes of myocardial infarction were evident. In only 2 of these 8 cases were serial electrocardiograms during anomalous atrioventricular excitation published, and in both cases an electrocardiogram was published, apparently from before and after the assumed date of infarction. These were Case 2 of Wolff and Richman,[11] and the case of Stein and Wróblewski.[9]

METHOD OF VECTOR ANALYSIS OF ELECTROCARDIOGRAMS

In accordance with modern electrocardiographic theory as propounded by Wilson and associates and by Bayley, the cardiac vector at any instant is a vector sum.[14,15] In 1933, Wolferth and Wood[16] suggested that the electrocardiogram in the WPW syndrome consists of the normal QRS and an early deflection representing early invasion of a certain section of the ventricles. Recently, Grant[17] has described the frequent occurrence of an additional depolarization abnormality, which he refers to as parietal block. Thus, the depolarization loop during anomalous atrioventricular excitation consists of three component, closed depolarization loops: the delta loop, the normal QRS loop, and the parietal-block loop when present. Symbolically,

$$E_{WPW} = \Delta + QRS + PB$$

From the Cardiopulmonary Laboratory of the Bishop Clarkson Memorial Hospital, and the Department of Medicine of the University of Nebraska College of Medicine, Omaha, Neb.

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where E_{WPW} is the cardiac vector during anomalous atrioventricular excitation, Δ is the delta vector, QRS is the normal QRS vector, and PB is the parietal-block vector at any instant during ventricular depolarization. The delta loop either may terminate in 0.05 or 0.06 second or may persist through most or all of the period of ventricular depolarization.

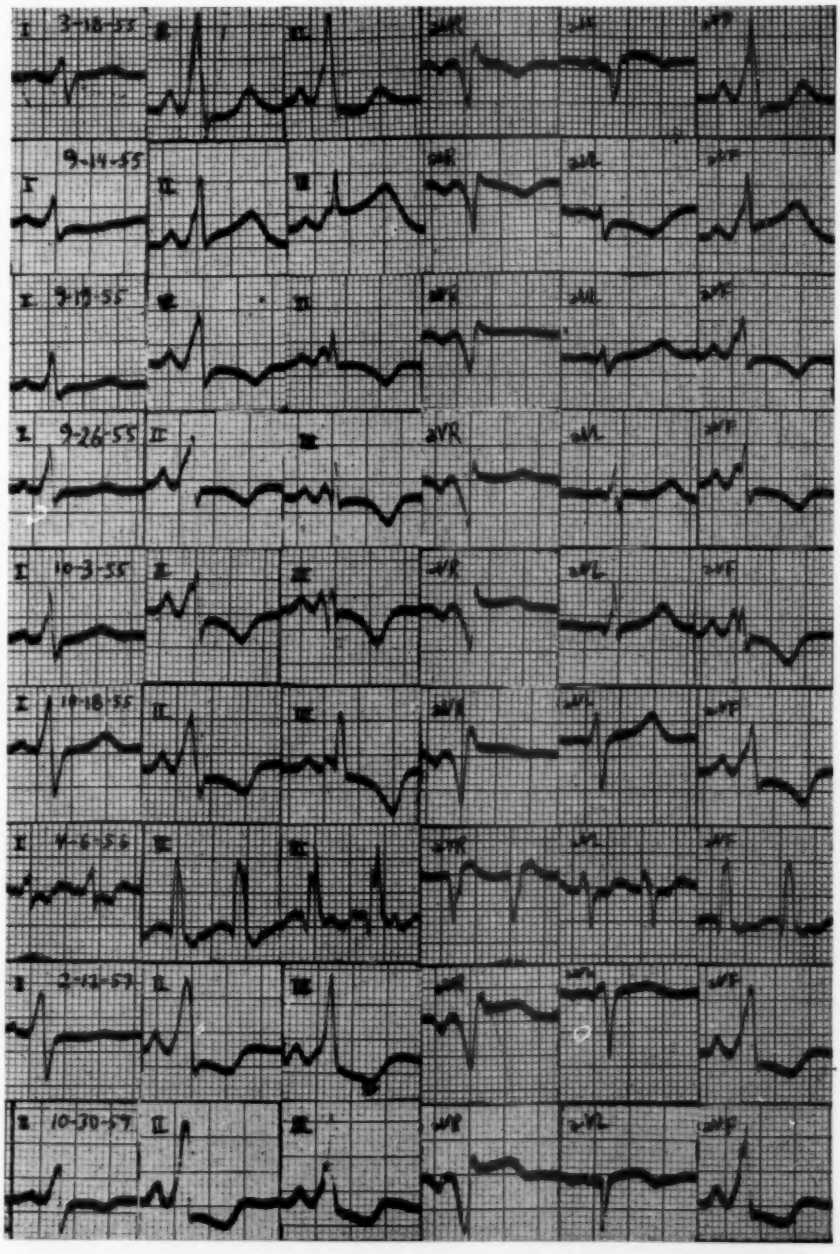

Fig. 1A.—Limb leads on nine different occasions. Clinically, the myocardial infarction occurred Sept. 14, 1955. The tracing dated April 6, 1956 was taken during a bout of supraventricular tachycardia with a ventricular rate of 165. Subsequently, the patient developed congestive failure and was digitalized. The ventricular rate on Oct. 18, 1955 was 60, and on Feb. 12, 1957, was 50.

The parietal-block loop may be limited to the last period of ventricular depolarization or may commence earlier, perhaps shortly after the onset of the delta loop, and persist through most or all of the period of ventricular depolarization. Parietal block may be etiologically related to the delta depolarization, to an interaction of the delta and QRS depolarizations, or to a combination of these and other factors. What is referred to as parietal block may not involve ventricular conduction fibers. Parietal block may occur anywhere in the ven-

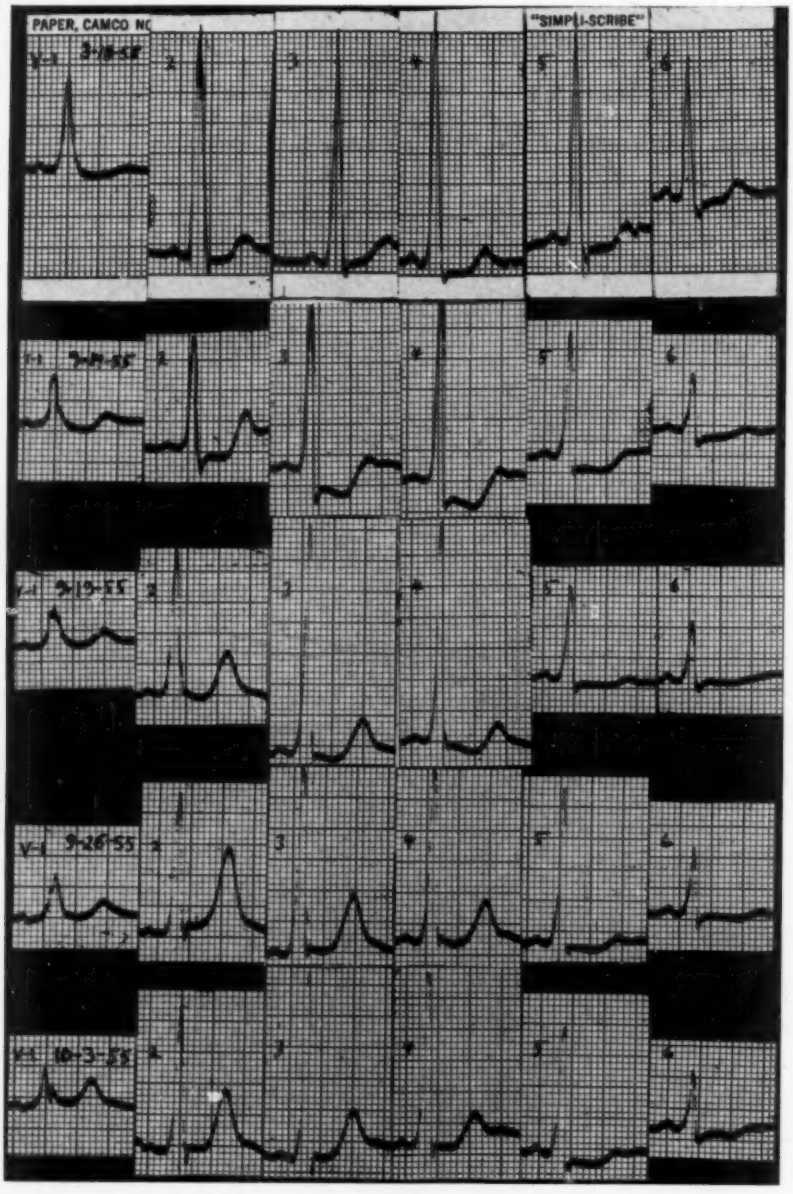

Fig. 1*B*.—Precordial leads from the first five electrocardiograms.

tricles and may represent more than one separate depolarization. Which of the preceding possibilities is true has little bearing on the utilization of the method of analysis to be presented for the recognition of myocardial infarction.

If the delta, QRS, and parietal-block components are unchanged on two electrocardiograms, the consideration of them is obviated by their cancellation by the method of vectorial subtraction to be presented. If they are changed between the two electrocardiograms, as for example by infarction, some consideration of them is both necessary and informative.

In accordance with modern electrocardiographic theory myocardial necrosis due to infarction may produce both early death vectors and late peri-infarction-block vectors. The characteristics of the peri-infarction-block vectors have been

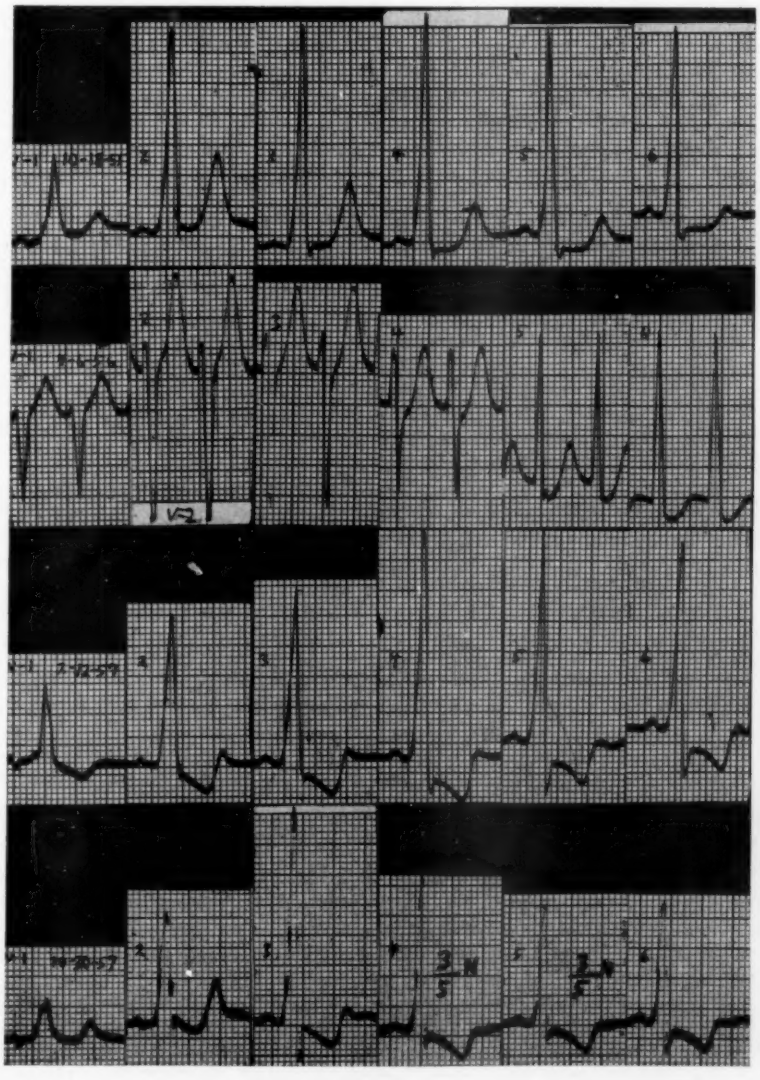

Fig. 1*C*.—Precordial leads from the last four electrocardiograms. On Oct. 30, 1957, Leads V_4 and V_5 were recorded at 0.6 normal standardization.

described by Grant and Murray.[18] After myocardial infarction in the presence of normal atrioventricular excitation the depolarization loop consists of three component, closed depolarization loops: the QRS-death loop, the normal QRS loop, and the peri-infarction-block loop when present. Symbolically,

$$E_I = QRS_d + QRS + PIB$$

where E_I is the cardiac vector, QRS_d is the QRS-death vector, and PIB is the peri-infarction-block vector at any instant during ventricular depolarization.

If myocardial infarction producing QRS-death vectors and peri-infarction-block vectors occurs in the presence of anomalous atrioventricular excitation with parietal block, all five components will be present. Symbolically,

$$E_{IWPW} = \Delta + QRS_d + QRS + PB + PIB$$

where E_{IWPW} is the cardiac vector during anomalous atrioventricular excitation following myocardial infarction at any instant during ventricular depolarization.

It seems further apparent that both the delta and parietal-block vectors are susceptible to change following infarction due to necrosis of myocardial or Purkinje fibers involved in their production. Consequently, we can revise the equation to account for the possible presence of vectors produced by defects in the wave fronts of the delta and parietal-block depolarizations due to the infarction. Symbolically,

$$E_{IWPW} = \Delta + \Delta d + QRS_d + QRS + PB + PB_d + PIB$$

where Δd is the delta-death vector and PB_d is the parietal-block-death vector at any instant during ventricular depolarization.

It follows that the electrocardiographic recognition of myocardial infarction during anomalous atrioventricular excitation may be based on the demonstration of any of the four groups of vectors or loops resulting from infarction, namely, the usual QRS-death and peri-infarction-block vectors and the particular delta- and parietal-block-death vectors. Assuming that an electrocardiogram taken after infarction shows a pattern resulting from the presence of all seven components described, while an electrocardiogram on the same patient prior to infarction shows a pattern due to the presence of delta, QRS, and parietal-block components, the difference between the two electrocardiograms must be due to the four infarction components. Symbolically, subtracing E_{WPW} from E_{IWPW} we have,

$$\begin{aligned} E_{IWPW} &= \Delta + \Delta d + QRS_d + QRS + PB + PB_d + PIB \\ E_{WPW} &= \Delta + QRS + PB \\ \hline E_{IWPW} - E_{WPW} &= \Delta d + QRS_d + PB_d + PIB \end{aligned}$$

Such subtraction can be done mentally, but is best done graphically. Vectorcardiograms can be constructed in the usual fashion from the electrocardiograms, and the preinfarct loop can be subtracted vectorially from the infarct loop. One of the easiest ways to do this is to rotate the preinfarct loop 180 degrees and then add corresponding instantaneous vectors from the two loops.

The resulting loop will consist of delta-death, QRS-death, parietal-block-death, and peri-infarction-block vectors, or any combination of them. If delta-death vectors are present, they can be recognized easily by their early appearance before the time of expected onset of QRS. They will, of course, continue beyond this time for a variable period. The QRS-death and peri-infarction-block vectors can be recognized in the usual fashion, since they will have the same characteristics they manifest in the absence of anomalous conduction. Any part of the loop unaccountable for as delta death, QRS death, or peri-infarction block will be classified by the process of elimination as parietal-block death.

If any of these components are absent, the analysis becomes simpler. If the electrocardiograms show no evidence of parietal block, and if there are no delta-death or peri-infarction-block vectors, the difference between the pre-infarct and infarct loops will be entirely due to QRS-death vectors. Symbolically,

$$\begin{aligned} & E_{IWPW} = \Delta + QRS_d + QRS \\ - \quad & E_{WPW} = \Delta + QRS \\ \hline & E_{IWPW} - E_{WPW} = QRS_d \end{aligned}$$

If an electrocardiogram prior to infarction is not available, the analysis can still be made if there are serial changes on two or more electrocardiograms taken after infarction. Under these circumstances the recognition of infarction involves the identification of serial change in any of the four infarction vectors mentioned above.

The presence of additional components, such as right or left ventricular hypertrophy, right bundle branch block, or delta- , QRS- or parietal-block-death or peri-infarction-block vectors from a previous infarction, will cause no difficulty, providing they are unchanged between the electrocardiograms being compared. Vectorial subtraction of the loops of two electrocardiograms will remove the vectors of all components which are unchanged on the two electrocardiograms.

CASE REPORT

The patient was first seen on March 18, 1955, at which time he was 49 years old. There were no cardiovascular complaints, and the physical examination was negative. An electrocardiogram was taken and showed the WPW syndrome.

On Sept. 14, 1955, the patient developed severe chest pain which radiated to both shoulders and down the left arm to the elbow. He was admitted to the Bishop Clarkson Memorial Hospital, Omaha, Neb. Morphine in large doses was necessary to control the pain. The white blood count shortly after admission was 19,500. The sedimentation rate on admission was 8 mm. per hour. It subsequently rose to 34 mm. per hour, and then fell successively to 20 and 17 mm. per hour. There was a very slight elevation of temperature initially. There were no bouts of arrhythmia or congestive failure. Serial electrocardiograms were taken and were interpreted by the author as showing the WPW syndrome and acute inferior wall myocardial infarction.

On April 6, 1956, the patient developed a bout of supraventricular tachycardia and was seen in his physicians' office, where an electrocardiogram revealed normal atrioventricular excitation.

In July, 1956, the patient developed congestive failure and was digitalized. The next electrocardiogram was taken on Feb. 12, 1957. The last electrocardiogram was taken on Oct. 30, 1957, during an admission for epididymitis.

The electrocardiograms are reproduced in Figs. 1*A*, 1*B*, and 1*C*.

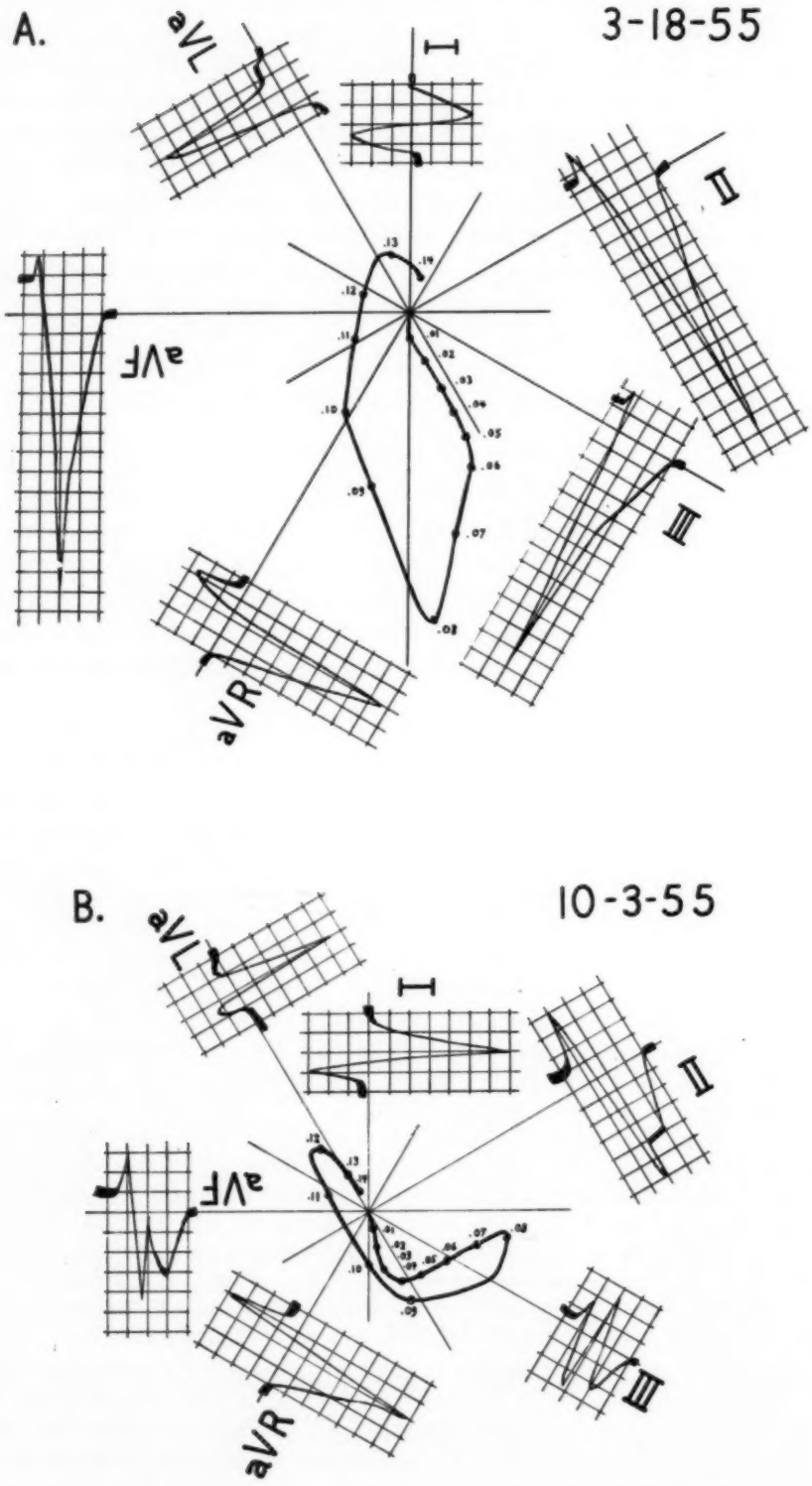

Fig. 2.—Derivation of frontal plane loops. *A*, March 18, 1955. *B*, Oct. 3, 1955.

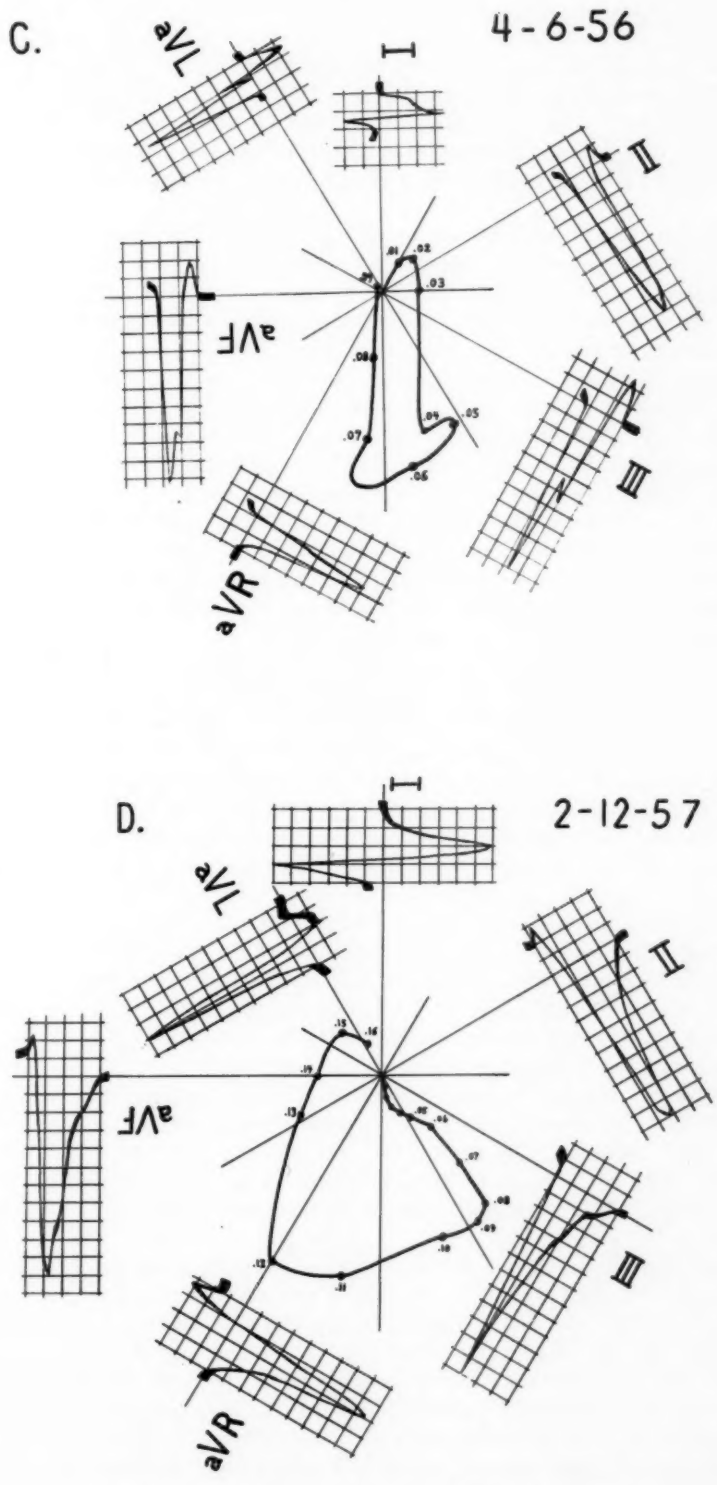

Fig. 2 Cont'd.—*C*, April 6, 1956. *D*, Feb. 12 1957.

ANALYSIS OF THE ELECTROCARDIOGRAMS

Derivation of the frontal plane loops for the electrocardiograms taken prior to infarction on March 18, 1955, and following infarction on Oct. 3, 1955 and Feb. 12, 1957, and during the bout of supraventricular tachycardia on April 6, 1956, is shown in detail in Fig. 2,*A-D*. For subsequent calculations slight alteration of the duration of depolarization and timing of the loops is necessary for April 6, 1956 and Feb. 12, 1957, because the heart rates on those dates were 165 and 50, respectively.

In Fig. 3,*A* the preinfarct WPW-syndrome loop and the infarct WPW-syndrome loop for Oct. 3, 1955, are superimposed. It is apparent that vectors from the preinfarct loop to equivalent points on the infarct loop will be directed upward and to the left. To show this more precisely, the loop resulting from vectorial subtraction of the two loops is shown in *B*. It can be seen that there are delta-death vectors present in the initial portion of the loop. They are directed upward and to the right. How long they persist cannot be determined precisely from study of this loop. It is necessary to have a normally excited electrocardiogram to compare with one taken during anomalous atrioventricular excitation in order to attempt to define the end of the delta loop, and this still may not be possible if there is parietal block. Subtracting what is arbitrarily considered to be the delta portion of one loop from the corresponding portion of another loop has left a remainder. By definition this remainder is the delta-death portion of the difference loop.

The next portion of the loop, from approximately 0.06 to 0.12 second, occurs at the appropriate time for QRS-death vectors and has the direction typical for inferoseptal infarction. The small terminal portion of the difference loop could represent continuing QRS-death vectors, parietal-block-death vectors, or peri-infarction-block vectors.

In Fig. 4, *A* the preinfarct WPW-syndrome loop and the infarct WPW-syndrome loop from Feb. 12, 1957, are superimposed. Time intervals of 0.01 second are indicated on the loops. In *B*, vectors are drawn from the termini of vectors of the preinfarct loop to termini of vectors of the infarct loop. Transposing these vectors so that they have a common origin gives the loop in *C*. The same loop is obtained by rotating the preinfarct loop 180 degrees and then adding successive vectors to those of the infarct loop. Looking at the loop in *C*, it is again apparent that there are delta-death vectors. QRS-death vectors are present from about 0.06 to 0.09 second and are of moderate magnitude. In addition, the terminal vectors are now larger and are directed downward and to the right. According to our method of analysis, these vectors could be either parietal-block-death vectors or peri-infarction-block vectors. Because of their orientation approximately 180 degrees away from the QRS-death loop, they have the characteristic of peri-infarction-block vectors. In *D* the directions of the three components are indicated by single vectors.

Cancellation of delta, QRS, and parietal-block components by vectorial subtraction of the preinfarct WPW-syndrome loop from an infarct WPW-syndrome loop has been carried out for the other electrocardiograms, and similar results were obtained.

If one attempts to make the analysis without utilizing the preinfarct WPW-syndrome electrocardiogram, the same result can still be obtained. For example, the loop obtained by subtracting the loop of Sept. 14, 1955 or Oct. 30, 1957 from that of Oct. 3, 1955 appears to consist mainly of large QRS-death vectors directed upward to the left. The difference loop between Oct. 3, 1955 and Oct. 18, 1955 appears to be due to the sudden appearance of large peri-infarction-block vectors.

In summary, analysis of the WPW-syndrome electrocardiograms suggests the following sequential events. On Sept. 14, 1955, delta-death vectors appear and they are directed upward and to the right. This orientation suggests a defect in a delta wave front spreading from the high septal mass toward an inferoseptal infarct. These delta-death vectors gradually decrease in magnitude during the subsequent period of observation. On Sept. 14, 1955, QRS-death vectors appear, also, and these are directed upward and to the left, as is typical for inferoseptal infarction. During the period of observation these vectors first increase in magnitude and then decrease markedly. On Oct. 18, 1955, vectors appear which are typical of peri-infarction block as seen with inferoseptal infarction. These vectors subsequently decrease in magnitude. The consistency of these sequential events, with the events so frequently observed with inferoseptal infarction in the absence of anomalous excitation, is evidence of the validity of the analysis.

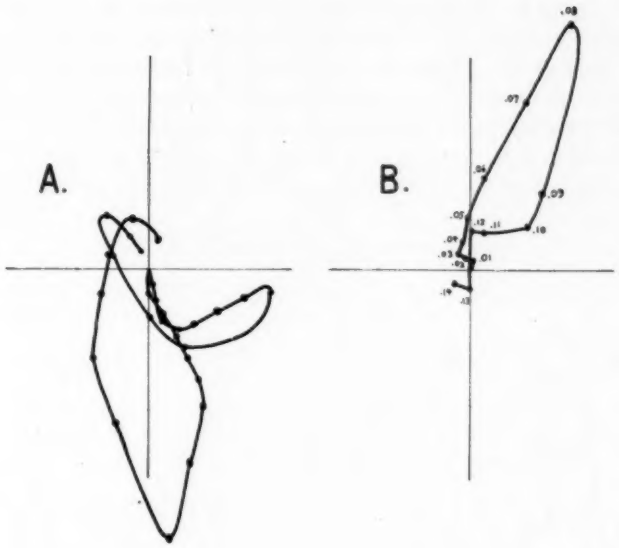

Fig. 3.—*A*, Preinfarct WPW-syndrome loop of March 18, 1955, and infarct WPW-syndrome loop of Oct. 3, 1955, superimposed (from Fig. 2, *A* and *B*). *B*, The loop resulting from vectorial subtraction.

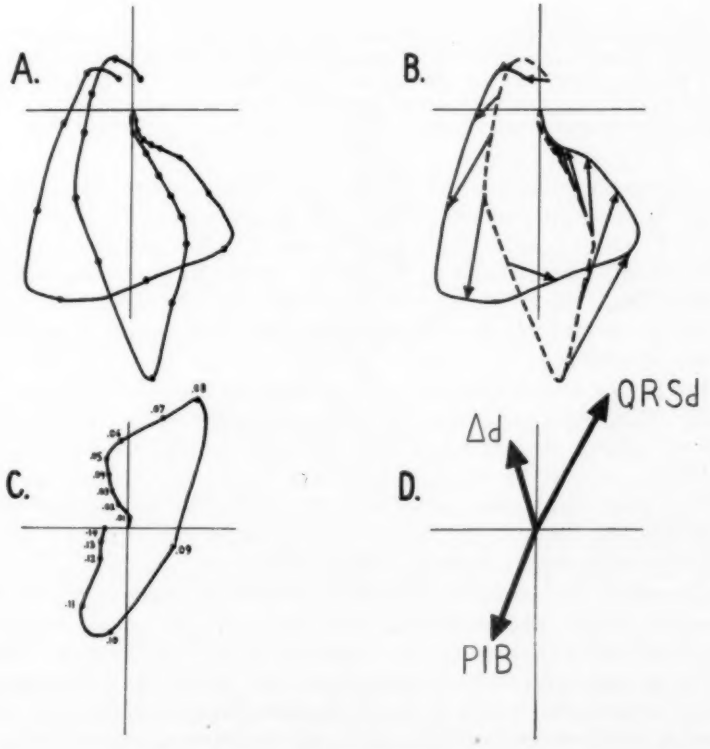

Fig. 4.—*A*, Preinfarct WPW-syndrome loop of March 18, 1955, and infarct WPW-syndrome loop of Feb. 12, 1957 (from Fig. 2, *A* and *D*). *B*, Vectors at 0.01-second interval from the preinfarct to the infarct WPW-syndrome loop. *C*, Difference loop obtained by transposing the vectors in *B* to have a common origin. *D*, Directions of the three components of the difference loop indicated by single vectors.

Further substantiation is obtained by turning to the normally excited electrocardiogram taken on April 6, 1956, during the bout of tachycardia. This electrocardiogram is interpreted as showing an old inferoseptal myocardial infarction with peri-infarction block, as manifested by the clockwise development of initial superiorly directed vectors, the deep notch on the central portion of the loop, and the rightward and inferiorly directed terminal forces.

If the analysis to this point is correct, it should be possible to subtract the derived QRS-death and peri-infarction-block loops from the loop of the normally excited electrocardiogram in order to obtain an artificially normal control QRS loop. Fig. 5,*A* shows the frontal plane loop for the normally excited infarct electrocardiogram as derived in Fig. 2,*C*. In Fig. 5,*B* is shown the

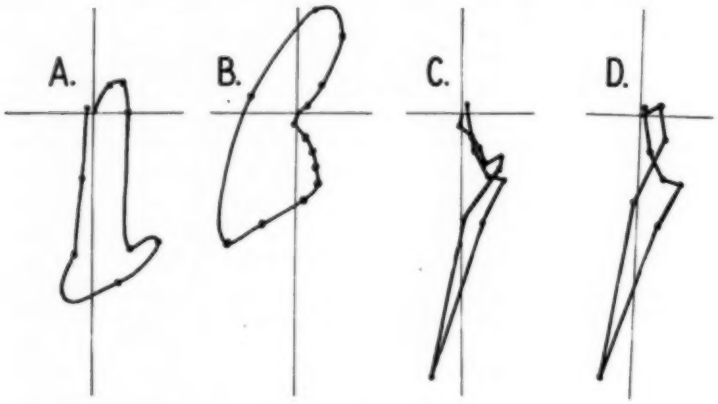

Fig. 5.—*A*, The loop during normal atrioventricular excitation after infarction (from Fig. 2, *C*). *B*, The difference loop between preinfarct WPW-syndrome loop of March 18, 1955, and infarct WPW-syndrome loop of Feb. 12, 1957, rotated 180 degrees (from Fig. 4, *C*). *C*, Loop obtained by adding *A* and *B*. *D*, Loop from *C* with first 0.05 second removed and loop closed. This loop consists of QRS and negative parietal-block-death components.

difference loop between the preinfarct and the infarct WPW-syndrome loops from Fig. 4,*C*, after this difference loop has been rotated 180 degrees. Vectorially adding the loops in *A* and *B* gives the loop shown in *C*, which consists of three components: QRS, and the negative delta-death and parietal-block-death vectors from Feb. 12, 1957 (see appendix for symbolic derivation). The first 0.05 second of this loop can be removed arbitrarily as representing negative delta-death vectors. The loop as shown in *D* then consists of QRS and any negative parietal-block-death vectors which may be present.

Although this derived control QRS may contain negative parietal-block-death vectors, there are certainly none approaching the magnitude of the parietal-block vectors themselves. To delineate the latter we subtract the loop for April 4, 1956 from the loop for Feb. 12, 1957, as shown in Fig. 6,*A*, in order to obtain the difference loop shown in *B*. This difference loop consists of delta as modified by delta death and parietal block as modified by any parietal-block-death vectors present (see appendix for symbolic derivation). Apparently, the large terminal portion of this loop is composed substantially of parietal-block vectors.

If one assumes that the parietal-block-death loop is either small or nil, the loop shown in Fig. 5,*D* becomes the single component QRS. The reasonableness of this derived control QRS is another way of defining a criterion for the proposed interpretive analysis. There are several factors making some inaccuracy difficult to avoid in this derivation. The electrocardiograms upon which the calculations are based, namely, those of March 18, 1955, April 4, 1956, and Feb. 12, 1957, were recorded at different heart rates, and during the interval between the last two electrocardiograms, the patient developed congestive heart failure.

As a result of the preceding analysis, dissection of any one of the infarct WPW-syndrome loops into its component loops can be attempted. This is done in an approximate fashion in Fig. 6,*C* for Feb. 12, 1957, for 6 components.

It is not necessary to derive accurately the vectorcardiogram in order to use the proposed method of analysis. Average or mean vectors for certain intervals of time during ventricular depolarization may be found by the method of Grant.[19] A vector representing the first 0.08 second and one for each of the two succeeding 0.04- or 0.05-second intervals will suffice for the case presented. In Fig. 7,*A* these three vectors are determined for the electrocardiogram of March 18, 1955, and in *B* they are determined for Feb. 12, 1957. In Fig. 7,*C*, vectors are constructed from the termini of the vectors for the preinfarct electrocardiogram to the termini of the vectors for the infarct electrocardiogram. In *D* these vectors are transposed to have a common origin, and they are considered to represent delta death, QRS death, and peri-infarction block, respectively. Comparison with Fig. 4,*C* and *D* indicates that this simplified approach gives results comparable to those obtained by the more tedious derivation of loops and their vectorial subtraction.

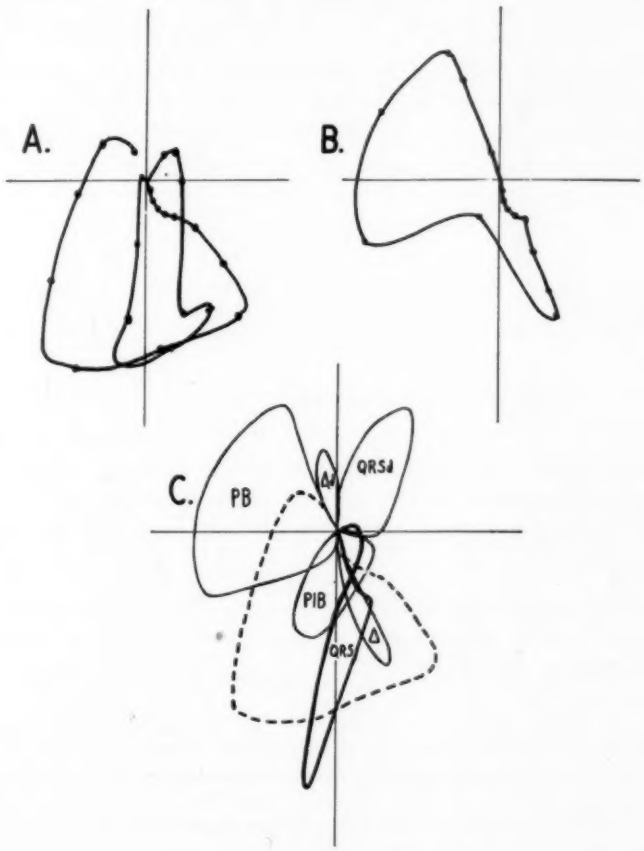

Fig. 6.—*A*, Loop during normal atrioventricular excitation and loop during anomalous excitation, both after infarction (from Fig. 2, *C* and *D*). *B*, The difference loop composed of delta, delta-death, parietal-block, and parietal-block-death components. *C*, Dashed line is the loop for Feb. 12, 1957 (from Fig. 2, *D*), and the solid loops are approximate component loops (from Fig. 4, *C*, Fig. 5, *D*, and Fig. 6, *B*).

Further confirmation of the diagnosis of inferoseptal myocardial infarction is to be had from study of the ST and T vectors. An equivalent systolic ST injury vector appears on Sept. 14, 1955, directed at +120 degrees, and on subsequent electrocardiograms it can be seen to decrease and disappear. The T vector at +100 degrees on Sept. 14, 1955, swings to −60 degrees on the next electrocardiogram, increases in magnitude on the ensuing three electrocardiograms, and then decreases. The orientation of ST and T vectors at +120 and −60 degrees is characteristic of inferoseptal infarction.

The primary nature of the T changes is revealed by a study of the ventricular gradient. Inspection of the electrocardiogram for March 18, 1955, reveals the spatial gradient to be about 35 microvolt seconds in magnitude and to be directed at about +80 degrees and moderately anterior. On Oct. 3, 1955, the spatial QRS vector has decreased in magnitude and has swung upward and to the left. Despite this the gradient with little change in magnitude has swung even farther upward and to the left, being at about −45 degrees and moderately anterior. On Feb. 12, 1957, with the patient on digitalis the gradient nearly disappears.

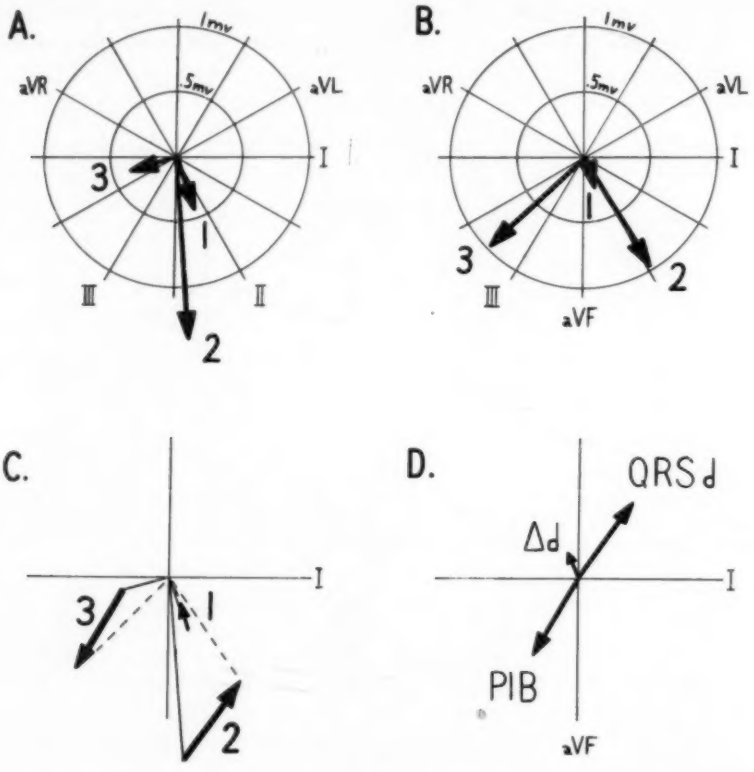

Fig. 7.—*A*, Mean vectors for the first 0.06-second and the succeeding two 0.04-second intervals from the preinfarct WPW-syndrome electrocardiogram taken March 18, 1955. *B*, Mean vectors for the first 0.06 second and the succeeding two 0.05-second intervals from the infarct WPW-syndrome electrocardiogram of Feb. 12, 1957. *C*, Vectors are constructed from the termini of the preinfarct to the termini of the infarct mean vectors. *D*, The vectors from *C*, transposed to have a common origin.

DISCUSSION

The method of vector analysis presented permits isolation of the component loop or loops responsible for notable difference between the loops of two electrocardiograms, regardless of the number of additional component loops represented in the two loops. Vectorial subtraction of the loops of any two electrocardiograms leaves a difference loop which consists of the component loops responsible for the change between the electrocardiograms. Care must be taken to avoid differences due to respiration or to changes in standardization or electrode placement.

In the case presented there appears to be a delta-death loop so oriented as to suggest that the delta wave front approaches the area of necrosis from above and to the right. This is suggestive of a high septal focus for the delta depolarization. The development of an inferoseptal QRS-death loop would seem to indicate that most of the inferoseptal wall is depolarized in the normal fashion rather than being involved in the delta depolarization.

Wolff and Richman[11] have stressed the variability of the ST-T in the WPW syndrome, and the consequent unreliability of ST-T changes in the diagnosis of myocardial infarction. The ST-T variations in the case presented appear to be reliable indications of inferoseptal myocardial infarction and, later, of digitalization, as demonstrated by study of the ventricular gradient.

The recognition of myocardial infarction from a single electrocardiogram with the WPW syndrome awaits the day when we have sufficient information about the normal characteristics of delta and parietal-block loops to permit their identification and differentiation from QRS-death and peri-infarction-block loops.

SUMMARY

The case presented is the third to be published with electrocardiograms recorded during anomalous atrioventricular excitation before and after myocardial infarction.

It is proposed that there are seven possible components to ventricular depolarization during anomalous atrioventricular excitation after myocardial infarction. A method of vector analysis is presented which permits selective vectorial cancellation of these components when they are manifested in two or more separate electrocardiograms. The characteristics of the four components which form the basis for the recognition of myocardial infarction are described.

The case presented is analyzed, and it is concluded that study of the ventricular depolarization loops for the electrocardiograms taken during anomalous atrioventricular excitation permits the recognition of the occurrence of an acute inferoseptal myocardial infarction. Analysis of the ST-T waves leads to the same conclusion. Analysis of an electrocardiogram taken during normal atrioventricular excitation appears to confirm the conclusions.

The author wishes to express his gratitude to Dr. F. W. Niehaus and Dr. W. D. Wright for permission to publish the case. Dr. Niehaus and Dr. Wright have been the patient's physicians throughout the period of observation.

APPENDIX

Symbolic derivation for loop shown in Fig. 5, *C*.

$$\begin{array}{rr} & E_{IWPW} = \Delta + \Delta d + QRS_d + QRS + PB + PB_d + PIB \\ - & E_{WPW} = \Delta + QRS + PB \\ \hline & E_{IWPW} - E_{WPW} = \Delta d + QRS_d + PB_d + PIB \end{array}$$

$$\begin{array}{rr} & E_I = QRS_d + QRS + PIB \\ - & E_{IWPW} - E_{WPW} = \Delta d + QRS_d + PB_d + PIB \\ \hline & E_I + E_{WPW} - E_{IWPW} = QRS - \Delta d - PB_d \end{array}$$

Symbolic derivation for loop shown in Fig. 6, *B*.

$$E_{IWPW} = \Delta + \Delta d + QRS_d + QRS + PB + PB_d + PIB$$

$$- \quad E_I = QRS_d + QRS + PIB$$

$$E_{IWPW} - E_I = \Delta + \Delta d + PB + PB_d$$

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"Cardio-Vocal Syndrome": Laryngeal Paralysis in Intrinsic Heart Disease

Harold H. Stocker, M.D., and H. T. Enterline, M.D., Philadelphia, Pa.

Vocal cord paralysis, bilateral or unilateral, is most commonly due to peripheral nerve injury caused by a malignant growth or by thyroid surgery.[3,9] Not uncommonly, however, a flaccid vocal cord, manifested symptomatically by hoarse speech, is a sign of cardiovascular disease. In such cases the cord involvement is unilateral, and it is almost always the lengthy and vulnerably positioned left recurrent laryngeal nerve that is implicated. Lesions of the aortic arch, such as aneurysm (syphilitic and atherosclerotic) and syphilitic aortitis unassociated with aneurysm, are responsible at times; but it is even more likely (at least in some locales) that the basic lesion is a form of intrinsic heart disease, such as mitral stenosis, a congenital cardiac defect, hypertensive heart disease, or coronary artery disease.[9]

An aneurysm of the aortic arch brings about fixation and stretching of the intimately associated left recurrent nerve, but the mechanism of nerve injury in cases of intrinsic heart disease has, for years, been a matter for consideration and is still open to dispute. That the pulmonary artery plays a crucial role in the mechanism is the consensus among authors who have studied the problem. Mitral stenosis is the intrinsic cardiac lesion most frequently associated with vocal cord paresis[9]; on the other hand, arteriosclerotic heart disease, as a primary diagnosis, is apparently very rarely a cause of this syndrome, only 2 such cases with autopsy confirmation and 2 other cases on a clinical basis having been reported. Thus, in consideration of the rarity of such reports, with a view toward furthering the cause of accurate diagnosis of such cases, and with the hope of adding something worth-while to the theories of the pathogenesis of the nerve injury, a third autopsy-confirmed case based on coronary artery disease is herein presented.

CASE REPORT

The patient (H.U.P. No. 56-431) was a 42-year-old white man, who had been a shop foreman for 18 years.

First Admission.—He was admitted to the Hospital of the University of Pennsylvania, to the private service of Dr. Joseph Atkins, on Oct. 4, 1956, with a chief complaint of hoarseness of 2 weeks' duration. He had suffered a severe myocardial infarction 2 years previously. Three

From the Department of Pathology, Hospital of the University of Pennsylvania, Philadelphia, Pa.
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months prior to the present admission he had had an attack of acute right upper quadrant pain, accompanied by a persistent and nonproductive cough. Then hoarseness occurred and became permanent.

Examination: The temperature, blood pressure, pulse, and respiratory rates were within normal limits. The examinations of the heart and lungs were normal also. The liver was moderately enlarged. Laryngoscopy by Dr. Atkins disclosed a "posticus paralysis of the left vocal cord with some loss of tension." Bronchoscopy and esophagoscopy were nonrevealing.

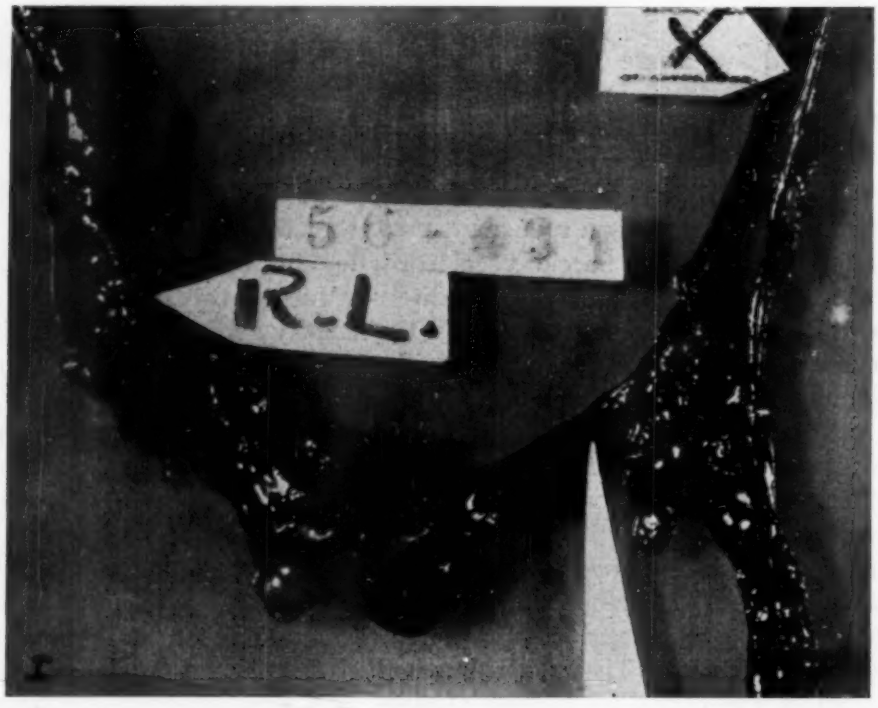

Fig. 1.—Left vagus and recurrent laryngeal nerves. Note dissolution of the recurrent nerve within its sheath (point of arrow) 1 cm. distal to its origin from nerve *X*, where it lies between the aorta and the pulmonary artery.

Laboratory data: The hemoglobin was 15 Gm. per cent and the white blood cell count was 12,600 with a normal differential. The Kolmer and Kline tests were not reactive. By x-ray examination the heart was top normal in size, and the pulmonary artery was not particularly prominent, even in retrospect. (All of the chest films were reviewed by Dr. Phillip Hodes and Dr. Roderick Tondreau of the Radiology Department of the Hospital of the University of Pennsylvania.) The swallowing function was normal by x-ray examination. The electrocardiogram indicated an old infarction anteriorly, and possibly posteriorly also.

Course: The hoarseness persisted, and he was discharged with the diagnosis of idiopathic left vocal cord paralysis.

Second Admission.—After discharge the patient felt fairly well for 3 weeks. Then nausea became troublesome, his cough reappeared, and he experienced some dyspnea. He was readmitted, this time to the medical ward service of Dr. Francis Wood.

Examination: The blood pressure was 90/80 mm. Hg, and the heart was regular at a rate of 100. A gallop rhythm was heard. The lungs were clear. The liver edge was slightly palpable, and there was 2+ ankle edema. The left vocal cord was again seen to be paralyzed, in adduction.

Laboratory data: The routine blood and urine studies were again normal. The basal metabolic rate was −18 per cent and −27 per cent. The prothrombin was 40 per cent. Extensive

blood studies, including hepatic tests, were essentially normal. The venous pressure was 18 cm. of water, and the circulation time from arm to tongue was 60 seconds. The chest x-rays showed a moderate increase in the size of the heart over a 5-week period. Again, the pulmonary artery was not unduly prominent. The electrocardiogram showed general decrease in voltage since the time of the previous admission. Right-sided cardiac catheterization revealed the following: The pressure in the pulmonary artery was 70/30 mm. Hg (normal: 15-25/5-10); in the right atrium, 20/15 mm. Hg (normal: 0-5); in the right ventricle, 70/15 mm. Hg (normal: 15-20/0-5); and the pulmonary artery wedge (capillary) pressure was 35/15 mm. Hg (normal: 5-10). The elevated pulmonary wedge pressure with a slightly increased pulmonary artery-pulmonary wedge pressure gradient suggested postpulmonic arteriolar type of pulmonary hypertension, such as is seen in cases of mitral valve disease or left ventricular failure.

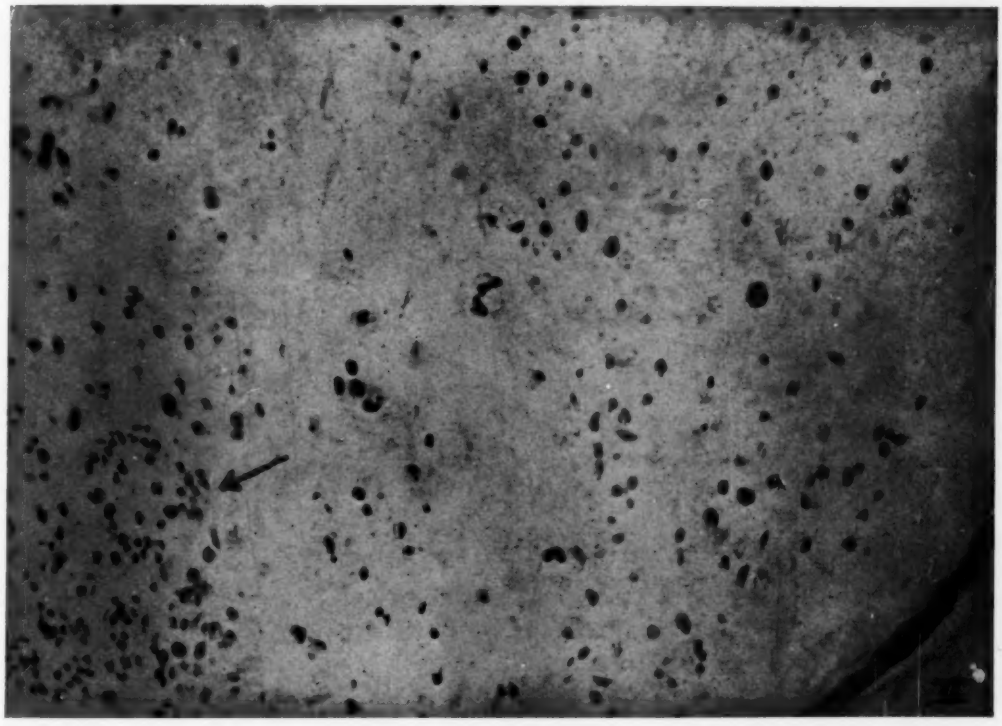

Fig. 2.—Left recurrent laryngeal nerve bundle, cross section, microscopic. The section was taken just distal to the point of injury. Note absence of axons, except for a few indicated by the arrow at lower left. (Bodian stain. Magnification × 500; reduced ¼.)

Course: The patient improved temporarily, with some loss of edema on a regimen consisting of bed rest, Digoxin, aminophylline, Thiomerin, and salt restriction. There was hemoptysis for the last 3 days. His death came suddenly without pulmonary edema on the twenty-fifth hospital day.

Autopsy.—The pertinent findings centered about the heart, the left recurrent laryngeal nerve, and the intrinsic muscles of the vocal cords.

The body was that of a fairly well-nourished adult white man. The weight was 68 kilograms and the length 178 cm. The right pleural cavity contained 350 c.c. of effusion fluid, the left, 300 c.c. The pleural surfaces were not remarkable and were without adhesions. The thyroid gland weighed 17 grams and was not remarkable grossly or histologically. The pericardial sac contained 150 c.c. of fluid, and the heart itself weighed 450 grams.

There were severe changes of atherosclerosis with calcification throughout the coronary artery tree, complicated by old occlusions of the anterior descending and circumflex coronary arteries

as well as by marked narrowing of the right coronary artery. There was dense fibrosis and narrowing of the anterior, apical, and posterior walls of the left ventricle, confirmed microscopically; no sign of recent infarction was seen. There was a 5 x 4 x 2 cm. organized thrombus in the left ventricle, tightly adherent to the septal and anterior portions of the apical wall. This thrombus was hollowed out. No peripheral emboli were found throughout the dissection.

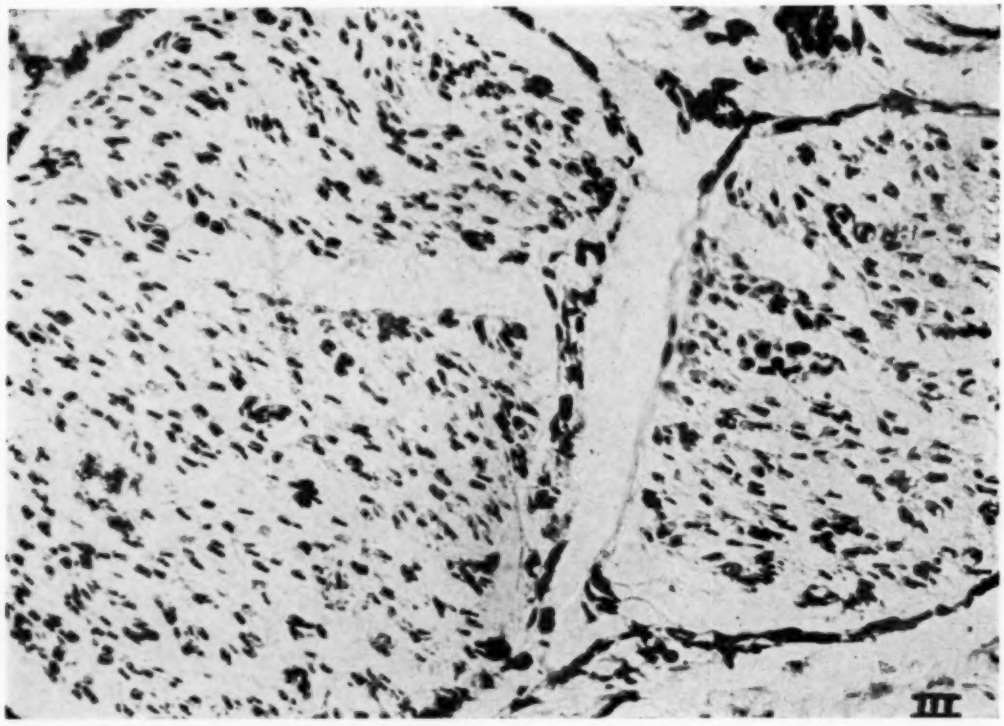

Fig. 3.—Normal control left recurrent laryngeal nerve bundle, microscopic. Note full complement of axons within the bundle. (Bodian stain. Magnification ×500; reduced ¼.)

The brain was not examined.

There was moderate hypertrophy and dilatation of the right ventricle, its wall measuring 5 to 6 mm. in thickness; it was thought that this alone explained the moderate cardiomegaly. There was no hypertrophy or dilatation of the left atrium, left ventricle, or right atrium. The valve ring measurements were within normal limits; the pulmonary valve ring was top normal at 8 cm. The valves themselves were not remarkable, nor was the pericardium. No anomalous vessel or congenital defect was noted. No tumor or amyloid deposits were found.

A number of small pulmonary emboli (2 to 4 mm.) were found in each lung; these appeared microscopically to range in age from very recent to a few weeks old. Distal to the emboli the pulmonary parenchyma was infarcted to the following extent: left lower lobe, 30 per cent; right lower lobe, 50 per cent; and right middle lobe, 30 per cent. Many pigment-laden cells (heart failure cells) were seen throughout the pulmonary parenchyma. The gross and microscopic appearance of the liver indicated chronic passive congestion.

The left recurrent laryngeal nerve was carefully dissected out. There was thinning of the nerve within the nerve sheath at the point where it passed between the aorta and the left pulmonary artery, adjacent to the ligamentum arteriosum (Fig. 1, point of arrow). Microscopically there was a complete loss of axons and myelin over some 70 to 80 per cent of the cross-sectional area of the combined nerve bundles in a section taken just distal to the observed gross lesion. A photomicrograph of a portion of one of the injured nerve bundles is shown in Fig. 2; the few re-

maining axons appear as black dots in the cross-sectional aspect. For comparison, a normal control section of a left recurrent laryngeal nerve was selected from another autopsy (Fig. 3). The left vagus nerve was normal grossly and histologically; a section of this nerve was taken just proximal to the origin of the left recurrent nerve.

There was moderate atherosclerosis of the aorta in the area of the ligamentum arteriosum, and a small calcific plaque was seen in the media in that portion of the wall in contiguity with the nerve. There was slight atherosclerotic change of the pulmonary artery without calcification and moderate basophilic change in the media. The ligamentum arteriosum was short (5 mm.) and tough. The small lymph nodes in the aortic window were not remarkable, and no adhesions were noted along the course of the left recurrent nerve.

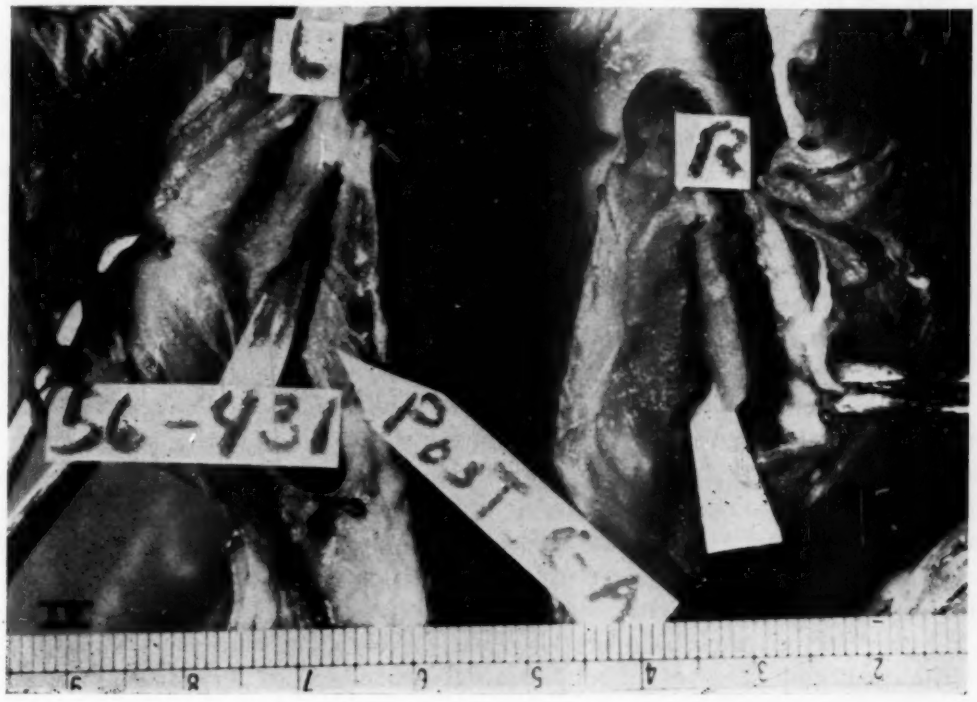

Fig. 4.—View of larynx, posterior. There is marked atrophy of the left posterior cricoarytenoid muscle

The vocal cords themselves were not remarkable grossly, but there was definite atrophy of two of the intrinsic muscles of the larynx. The left posterior cricoarytenoid muscle (vocal cord abductor) measured 2 mm. in thickness at its mid-point, whereas the corresponding muscle on the right was 5 mm. thick (Fig. 4). Microscopically, the left posterior cricoarytenoid muscle showed definite changes of atrophy, with loss of muscle bundles, decrease in size of many of the muscle bundles, and attempts at regeneration; the right muscle appeared healthy. The transverse and lateral cricoarytenoid muscles (vocal cord adductors) were also dissected out, and the same atrophic changes were noted, to a moderate degree, in the left lateral cricoarytenoid muscle. The transverse cricoarytenoid muscle was normal both on the right and the left.

DISCUSSION

Types of Intrinsic Heart Disease.—

1. *Mitral stenosis:* The association of left vocal cord paralysis with mitral stenosis has been recognized for 60 years, the original report being that of Ortner,[14]

who, in 1897, described 2 autopsy cases and assigned the observed degeneration of the left recurrent laryngeal nerve to direct pressure by an enlarged left atrium. Since the appearance of Ortner's classic description, a number of similar cases have been studied, but the mechanism of the nerve injury proposed by Ortner has not been accepted by later investigators. Instead, the factor of pulmonary artery dilatation has received the major attention, and a fair amount of circumstantial evidence now exists pointing to compression of the nerve between a dilated pulmonary artery and the aorta, at least in many cases. The importance of pulmonary artery dilatation was first proposed on the basis of x-ray findings, in 1904, by Alexander,[1] and autopsy corroboration first appeared the next year.[8] Fetterolf and Norris,[7] in 1911, studied carefully the normal anatomy of the area in question in an unstated number of Formalin-fixed cadavers, and they also reviewed the 11 autopsied cases and 26 clinical cases reported to that date, all with a diagnosis of mitral stenosis. They came to the conclusion that "when compression is accountable for recurrent paralysis, it must always be caused by the nerve being squeezed between the pulmonary artery and the aorta or the aortic ligament. Anything which will dilate or force upward the left auricle, the left pulmonary vein, or the left pulmonary artery would tend to cause the condition." They stated, as a finding from their studies, that the distance between the aorta and the left pulmonary artery in the aortic window is 4 millimeters.

On the basis of chest films and autopsy studies many authors have incriminated a dilated pulmonary artery as almost a sine qua non in this syndrome, and relatively recently this viewpoint has received added backing from observations based on angiocardiography,[18] cardiac catheterization,[11] and pressure measurements at operation.[11] Two catheterized cases with mitral stenosis had systolic pressures in the pulmonary artery of 43 and 41 mm. Hg (twice normal), and at operation a similar case had a pressure of 40 mm. Hg.

Other factors have been proposed as possibly significant in the production of the syndrome, such as inflammation (lymphadenitis, pericarditis), pressure from the left bronchus, right ventricular hypertrophy, pulmonary artery atherosclerosis, and the position of the ligamentum arteriosum. Dolowitz and Lewis[5] thought that lymphadenopathy, in the form of hypertrophy or scarring within the aortic window, might cause fixation of the nerve in specific cases. They found adherent nodes in the area in 4 cases in their anatomic study of 27 normal cadavers. There are no autopsy data concerning their 2 reported cases. Notkin[13] had previously suggested that a strategically placed lymph node might, at times, play an important role, since in his autopsied case with mitral stenosis such a node was found.

One author[15] reported the occurrence of bilateral vocal cord paralysis with mitral stenosis in 7 cases. A possible mechanism of nerve injury in such cases is difficult to imagine. No autopsy data are available; thus, interpretation should be cautious.

2. *Left ventricular failure:* King, Hitzig, and Fishberg,[10] in 1934, were the first to call attention to the occurrence of vocal cord palsy in left ventricular failure, not associated with rheumatic heart disease. They presented 3 patients,

2 of whom had suffered coronary occlusions and 1 who had severe hypertension. Post-mortem studies were presented in reference to the hypertensive case and one of the cases of myocardial infarction. In both, engorgement of the pulmonary vessels was seen on chest films, and, on autopsy, degeneration of the recurrent laryngeal nerve was seen histologically at the point where the nerve passes between the aorta and the left pulmonary artery and distal to it. The pulmonary artery was not dilated at autopsy in either case. The authors proposed a "dynamic dilatation" (during life) causing compression of the nerve against the aorta or ligamentum arteriosum, with resultant degeneration.

Only 3 additional reports have appeared concerning this syndrome with left ventricular failure,[4,17,20] one of which included post-mortem findings (Tashnek[17]). Tashnek concluded, in reference to his autopsied case with a myocardial infarction, that the observed nerve injury was probably due to pulmonary artery dilatation, since no other factor was present. No mention was made of the size of the pulmonary artery on x-ray examination or whether or not it was dilated at necropsy. Zelman and Nice's[20] clinical case of myocardial infarction displayed a low aortic arch on the chest film, and they thought that this might be an etiologic factor. The size of the pulmonary artery on the chest film was not mentioned, but the heart was large and the left atrium was prominent on fluoroscopy. In Diefenbach's[4] report of 2 clinical cases of hypertension no special mention was made of the size of the pulmonary artery on the chest films, but each patient had a large heart.

3. *Congenital cardiac defects:* Left laryngeal palsy has also been reported a number of times with various types of congenital cardiac lesions, such as atrial septal defect,[5,6] patent ductus arteriosus,[12] and Eisenmenger's complex.[16] These conditions have in common high pulmonary artery pressures, and often the pulmonary artery is grossly dilated at autopsy. In some of these cases hoarseness has begun almost at birth.

4. *Essential pulmonary hypertension:* Strangely enough, there has been only one report of vocal cord paralysis in "essential" pulmonary hypertension, the autopsy disclosing a much dilated pulmonary artery.[2]

Consideration of Mechanisms.—The fact that vocal cord paralysis is reported to be quite uncommon in mitral stenosis (0.5 per cent[11]), as well as in other types of intrinsic heart disease, suggests that dilatation or upward displacement of the pulmonary artery, of itself, does not suffice to cause the lesion, at least in most cases. Fetterolf and Norris stressed the "squeezing" of the nerve against the aorta or ligamentum arteriosum either by the pulmonary artery itself or through secondary pressure exerted from below by enlargement of hollow and distensible structures, such as the left atrium. Malcomson and Hillman[11] narrowed the point of focus still further and stressed the importance and constancy of a dilated pulmonary artery under increased tension. However, if one assigns sole importance to the presence of a dilated structure causing compression of the nerve, one then has difficulty explaining why hoarseness is so infrequently associated with known cases of dilatation of the pulmonary artery, enlargement of the left atrium, cardiomegaly, etc. Thus, it remains to be shown what the factor

is that determines in which cases the nerve shall be injured appreciably, once the pulmonary artery is dilated or displaced upward.

Various suggestions have been made as to possible mechanisms of nerve injury, some of which are mentioned above. One or more of these may be important, perhaps serving an ancillary role to the factor of pulmonary artery dilatation. The variation in the attachment of the ductus arteriosus might play a role.[19] Lymphadenopathy in the aortic window has been cited above. The possibility of the lesion being caused by stretching of the nerve after fixation at the aortic window has been set forth. It would seem reasonable that an ancillary factor need not be sought in cases of extreme pulmonary artery dilatation, such as are seen in relation to certain types of congenital cardiac defects.

The case reported herein tends to substantiate the importance of increased pulmonary artery pressure, since by cardiac catheterization the pressure in this vessel was 2 to 3 times normal. There was only slight to moderate cardiomegaly, due to hypertrophy of the right ventricular wall, and the left atrium was not dilated or hypertrophied. Despite increased pressure in the pulmonary artery, dilatation of this vessel was not noticeable on the chest films nor was it significantly present at autopsy. Thus, the x-rays offered no help in the diagnosis in this case. Perhaps there was sufficient dilatation of the pulmonary artery during life, particularly during systole, to bring about nerve damage but not enough to be conspicuous on x-ray examination.

Frequency of Left Laryngeal Nerve Injury.—As mentioned above, vocal cord paralysis has been reported as an infrequent complication of intrinsic heart disease. However, it is probable that certain instances of injury to the nerve, such as partial or slow injury, go undetected, since hoarseness may be absent or minimal in such cases. By visualization of the larynx, one can at times detect faulty movements of a cord when the voice is normal or nearly so.[3] Thus, the low percentage of vocal cord palsies recorded in intrinsic heart disease may not give an accurate estimation of the actual frequency of nerve injury. Perhaps visualization of the vocal cords should be a more common practice in the presence of heart disease. The finding of a weak or paralyzed left vocal cord could be taken as suggestive evidence of increased pulmonary artery pressure.

In large series of cases of vocal cord paralysis a very high percentage remains unexplained as to basic etiology (e.g., 28 per cent of 633 cases[9]). One wonders how many of these "idiopathic palsies," when affecting the left cord only, are actually attributable to cardiac disease, which may go unrecognized or unappreciated as a causative factor in the palsy. In some instances, hoarseness, due to left vocal cord difficulties, has been an early symptom of cardiac decompensation and has constituted the chief complaint at the initial medical visit.

"*Cardio-Vocal Syndrome.*"—The eponym "Ortner's syndrome" has been used occasionally, particularly in the European reports, but it is not found extensively in the literature. The term "cardio-vocal syndrome" is hereby proposed, in the interest of descriptive and brief nomenclature, to be used in reference to those cases of left laryngeal nerve palsy or paresis that are related to intrinsic heart disease and not primarily to extrinsic lesions such as aortic aneurysm, tumor, or cicatrizing processes.

SUMMARY

1. A case of occlusive coronary artery disease complicated by hoarseness due to left recurrent laryngeal nerve damage is presented. This is the third such autopsy case to be reported.

2. Hoarseness was an early symptom of cardiac decompensation, and, initially, it constituted the patient's chief complaint.

3. It is thought that nerve compression between the aorta and a dilated pulmonary artery is a constant factor in the production of recurrent nerve injury in cases of intrinsic heart disease. Dilatation of the pulmonary artery is at times noticeable on the chest film.

However, an additional unknown factor appears necessary to explain the pathogenesis, since dilatation of the pulmonary artery is apparently only rarely accompanied by significant damage to the recurrent nerve.

ADDENDUM

Recently, one of us (H.S.) observed a clinic patient, an 80-year-old white woman (Stanford University Hospital No. A-57006), who presented with a complete paralysis of the left vocal cord and was found to be in atrial fibrillation and left ventricular failure; the presumptive clinical diagnosis was atherosclerotic heart disease. There was no sign of mitral stenosis, aneurysm, etc., and the pulmonary artery was not dilated by x-ray examination.

We wish to thank Drs. Warner F. Sheldon, John J. Sayen, Lawrence Barrows, and David A. Rytand for expert assistance in the preparation of this report.

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Isolated Dextrocardia Associated With Lutembacher's Syndrome

N. R. Rowell, M.B., M.R.C.P., D.C.H., and W. J. S. Still, M.B., Ch.B.
Newcastle upon Tyne, England

The association of isolated dextrocardia and Lutembacher's syndrome has been reported on only one previous occasion (Innerfield[1]), and it is therefore a rare combination. Innerfield's communication was based on a clinical diagnosis aided by cardiac catheterization. In the present case the heart was available for study, post mortem.

CASE REPORT

E. R., a 53-year-old housewife, was admitted to the Royal Victoria Infirmary, Newcastle upon Tyne, in April, 1956, in severe cardiac failure. She had had acute rheumatism at 15 years of age, and first began to have palpitations and some nocturnal breathlessness at 20 years of age. Nevertheless, she had two normal pregnancies at 31 and 35 years of age. Admission to hospital was twice required at the age of 48 for episodes of cardiac failure, which responded to treatment with digitalis and diuretics. At that time a diagnosis of dextrocardia with atrial septal defect was made. Six weeks before the final admission to hospital, ankle swelling and increasing breathlessness occurred following a respiratory infection. At no time was there any hemoptysis. There was no family history of cardiac disease.

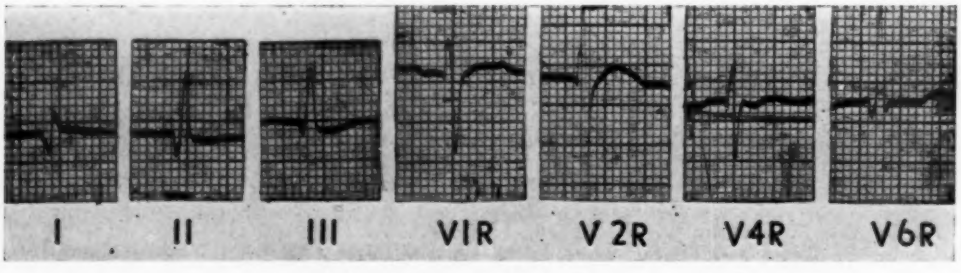

Fig. 1.—Electrocardiogram with V leads taken on the right side of the chest.

On admission she was in severe cardiac failure with orthopnea and slight cyanosis. The pulse was regular, 88 beats per minute, and the blood pressure was 105/60 mm. Hg. The apex was in the sixth right intercostal space, 14 cm. from the midline. There was a systolic thrill and murmur on both sides of the upper sternum, the murmur extending over the whole of the precordium

From the Departments of Medicine and Pathology, Royal Victoria Infirmary, Newcastle upon Tyne, England.
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and into the neck. A blowing diastolic murmur was also audible over the precordium, maximal at the left border of the sternum. An electrocardiogram (Fig. 1) showed inversion of all complexes in Lead I, with transposition of Leads II and III. Sinus rhythm was present with frequent auricular ectopic beats. The P waves were very small.

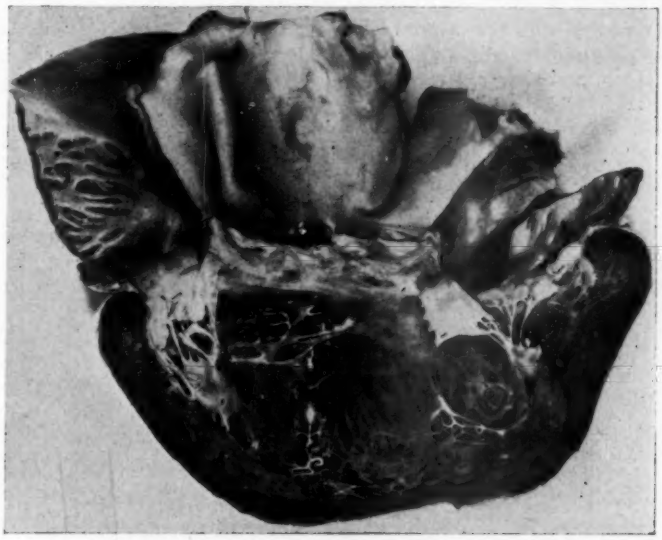

Fig. 2.

Fig. 3.

Fig. 2.—The right ventricle, and the pulmonary valve and artery are shown. Endocardial thickening is present proximal to the valve.

Fig. 3.—The foramen ovale is patent. The hypertrophied and dilated right atrium is seen posteriorly.

The patient did not respond to treatment and died 2 days after admission.

Autopsy Findings.—The heart weighed 750 grams, and displayed an isolated dextrocardia of the mirrored inversion type, with the arterial chambers on the right, the venous chambers on the left, and the apex pointing downward and to the right.[2] The ascending aorta passed ventrally over the right bronchus and then downward on the left side.

The anterior surface of the heart was composed of an enormously dilated and hypertrophied right ventricle, the wall of which measured 14 to 15 mm. at its greatest. The endocardium showed diffuse thickening proximal to the pulmonary valve, with two distinct endocardial "pockets"

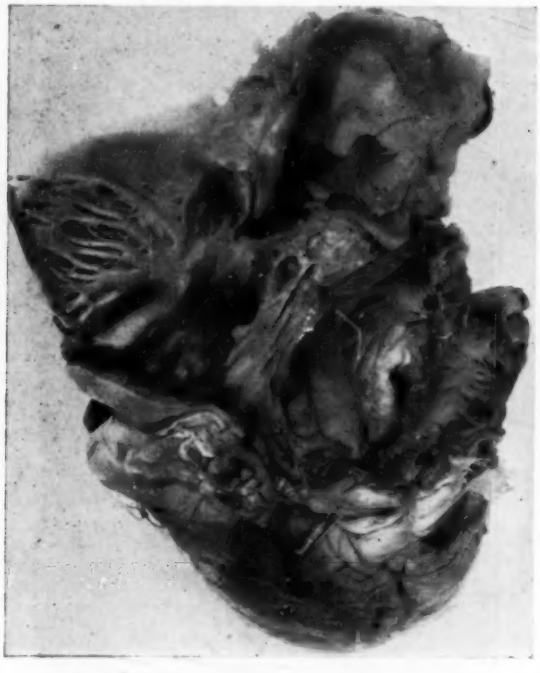

Fig. 4.—The left atrium is seen from above, with the stenosed mitral valve.

in this area, indicating incompetence of the distal valve. The pulmonary valve ring was dilated and the edges of its leaflets slightly thickened. The valve led, in turn, into a dilated pulmonary artery, which in its first part was almost aneurysmal in appearance (Fig. 2). This dilatation continued throughout the pulmonary vascular system.

The right atrium was dilated and hypertrophied, and although the leaflets of the tricuspid valve were normal, the valve ring was dilated, with consequent incompetence. The foramen ovale was widely patent and the opening edged by thickened endocardium (Fig. 3). The left atrium was approximately half the size of the right, but the endocardium in this chamber was diffusely thickened, and it led into a mitral valve which showed a "button hole" type of stenosis (Fig. 4). Histologic examination confirmed that the stenosis was rheumatic in origin. The left ventricle and aortic valve appeared normal. The only other relevant finding was a centrilobular hepatic fibrosis presumed to be cardiac in origin.

DISCUSSION

A case of Lutembacher's syndrome associated with isolated dextrocardia is described. The rheumatic nature of the mitral stenosis in this case, suspected on the clinical history, was confirmed histologically.

The diagnosis of Lutembacher's syndrome is usually difficult, and the characteristic diastolic murmur of mitral stenosis cannot always be heard. When dextrocardia complicates the picture, the origin of the murmurs becomes even more obscure. In this case the diastolic murmur heard at the left border of the sternum was attributed to aortic incompetence, when, in fact, it was due to incompetence of the pulmonary valve.

The lesions of uncomplicated Lutembacher's syndrome are usually well tolerated, and although the average age at death in McGinn and White's[3] series was 35 years, a patient described by Firket[4] survived for 74 years and had 11 pregnancies. There is no evidence that isolated dextrocardia alters the expectation of life[5]; the present patient survived for 53 years and tolerated 2 pregnancies.

SUMMARY

A case of isolated dextrocardia associated with Lutembacher's syndrome is described.

We wish to thank Dr. H. A. Dewar for permission to publish this case, and Mr. A. E. Young for the photographs.

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The Value of Aortic and Radial Pressure Pulses in the Diagnosis of Cardiovascular Disorders

J. Leo Wright, M.D., and Earl H. Wood, M.D.***
Memphis, Tenn., and Rochester, Minn.

The use of peripheral pulse contours alone as an aid in the diagnosis of cardiovascular disorders often is inconclusive.

Studies to determine whether the diagnostic accuracy of intra-arterial pressure pulses could be augmented by comparing the aortic contour with the radial pressure pulse generated by the same heart beat were conducted in 66 individuals. In addition to the control group of healthy subjects (15), patients with valvular aortic stenosis (25), aortic insufficiency (10), subvalvular aortic stenosis (1), coarctation of the aorta (5), mitral stenosis (5), and mitral insufficiency (5) were included.

In patients with valvular aortic stenosis, central and peripheral pulses were characterized by marked similarity in contour, prolonged build-up times, absence of the small postdicrotic oscillation usually noted on the aortic contour in healthy subjects, and absence of the radial systolic pressure increase (in 23 patients).

In severe aortic insufficiency, pressure pulses were characterized by a marked change in contour often associated with a marked increase in systolic pressure at the periphery. (A systolic pressure decrease was recorded in 1 patient.) Absence of the aortic postdicrotic wave and slurring of the dicrotic halt was noted.

In the patient with surgically proved subvalvular aortic stenosis, the presence of the small postdicrotic wave on the aortic contour suggested the presence of a normally functioning aortic valve.

Patients with coarctation (*above the site of coarctation*), mitral stenosis, and mitral insufficiency failed to show pressure pulse abnormalities diagnostic of these lesions.

It is suggested that analysis of both the aortic and radial pulse contours enhance the diagnostic discrimination of intra-arterial pressure pulses.

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*Cardio-Pulmonary Laboratory, Baptist Memorial Hospital, Memphis, Tenn.
**Section of Physiology, Mayo Clinic, Rochester, Minn.

A Study of Cardiac Vectors in the Frontal Plane

Zang Z. Zao, M.D., George R. Herrmann, M.D., and Milton R. Hejtmancik, M.D.
Galveston, Tex.

In clinical electrocardiography Einthoven, Fahr, and de Waart[1] assumed that the three limb electrodes, R, L, and F, were equidistant from each other and from the heart, that the heart was a fixed-point source of the electromotive field, and that the interposed tissue between heart and electrodes was homogeneous and of large dimension. The geometric consequence of this assumption is a circular disc, in which the center may represent the origin of the heart vector. The three electrodes, situated at the corners of the disc, if connected, form the famous equilateral triangle of Einthoven.

In their assumption the relation between lead polarity and heart vector direction may be expressed geometrically by a polarity circle of that lead.[2] A polarity circle is composed of a positive semicircle, a negative semicircle, and two zero-potential boundaries. If an electrocardiographic deflection is positive in a given lead, the heart vector direction resides in the positive semicircle of that lead; if negative, it is in the negative semicircle; and if it is zero potential or transitional, the direction coincides with one of the two boundaries. This is, of course, valid for any deflection, P, QRS, ST, T, whether it be a mean, main, or instantaneous vector.

The polarity circle of a lead may be constructed by drawing a positive semicircle to face the positive electrode and a negative semicircle to face the negative electrode. A line joining the two zero-potential boundaries would be perpendicular to that lead axis.

THE CIRCULAR FORM

Fig. 2 shows the rudiment of the circular form. It contains the polarity circles of the six limb leads within a circular disc. Each polarity circle was constructed in the manner described above. For example, in the circle of Lead I the positive semicircle (white) faces the electrode L, the negative semicircle (stippled) faces the electrode R, and a line joining the two zero-potential boundaries would be perpendicular to the Lead I axis. In Lead aV_R the positive semicircle faces

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the electrode R, the negative semicircle faces the geometric center (the Wilson central terminal is an extension of the Einthoven assumption, and therefore coincides with the geometric center), and a line joining the two zero-potential boundaries would be perpendicular to the Lead aV_R axis.

Fig. 1 shows the circular form, constructed by concentric arrangement of the six polarity circles from the rudiment. They represent, from within outward, limb Leads I, II, III, R (aV_R), L (aV_L), and F (aV_F). By such an arrangement it becomes obvious that polarities written in the six limb leads and the corresponding heart-vector direction can be correlated visually at a glance. If there is no zero potential (or transitional complex) written in any limb lead, the direction is, for the sake of simplicity and uniformity, assumed as being midway at 30 degrees in the appropriate sector. Thus, this form gives altogether 24 directions, each being separated by 15 degrees from the neighboring one, as indicated at the periphery.

Fig. 1.

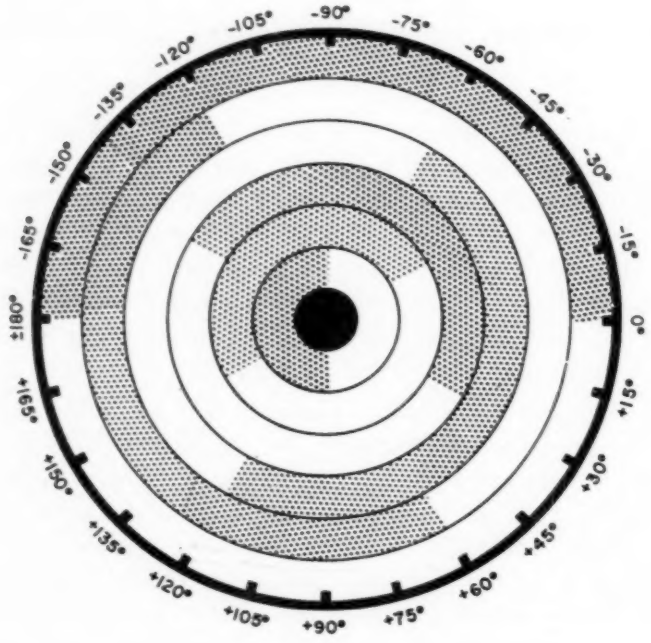


Fig. 2.

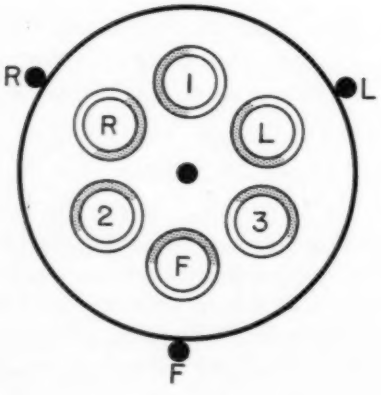
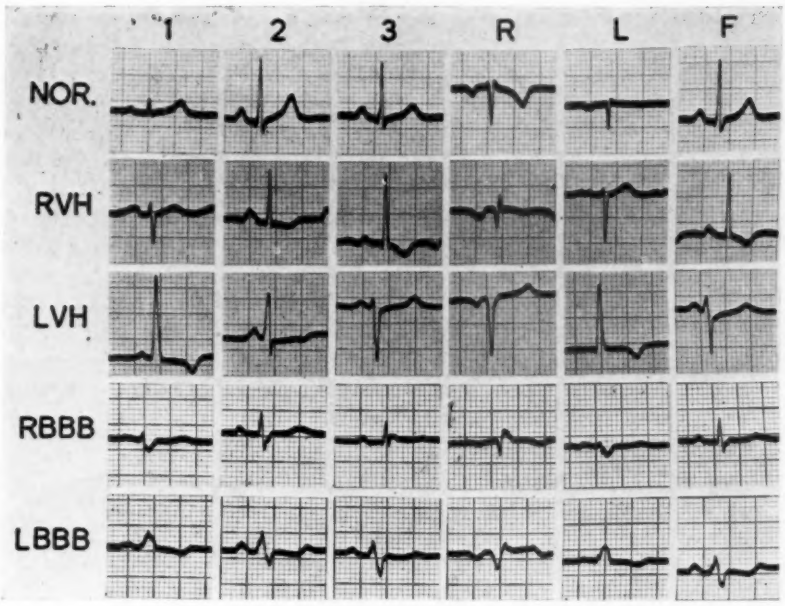
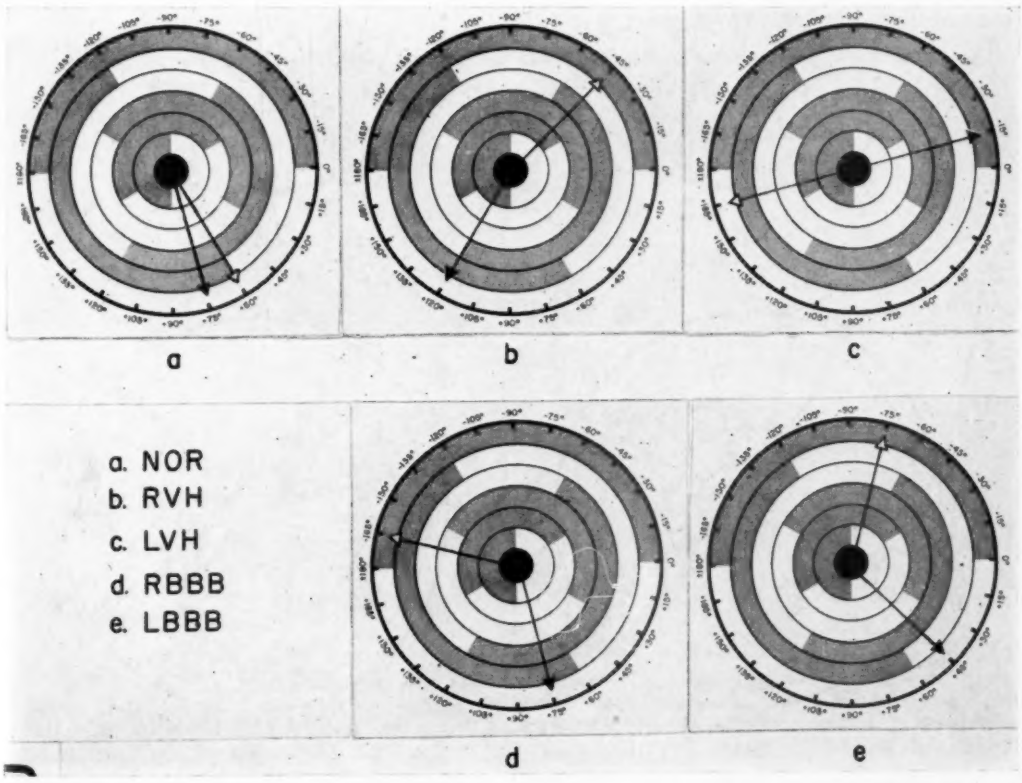


Fig. 1.—The circular form. The six concentric circles represent, from within outward, limb Leads I, II, III, R, L, and F. Positive semicircle is white, negative semicircle is stippled.

Fig. 2.—The rudiment of the circular form.



A.



B.

Fig. 3.—*A*, Limb lead electrocardiograms. *B*, Corresponding directions of the vectors of QRS, T, QRS′, and QRS″ obtained in the circular form. Each arrow indicates a vectorial direction: black for QRS or QRS′, white for T or QRS″.

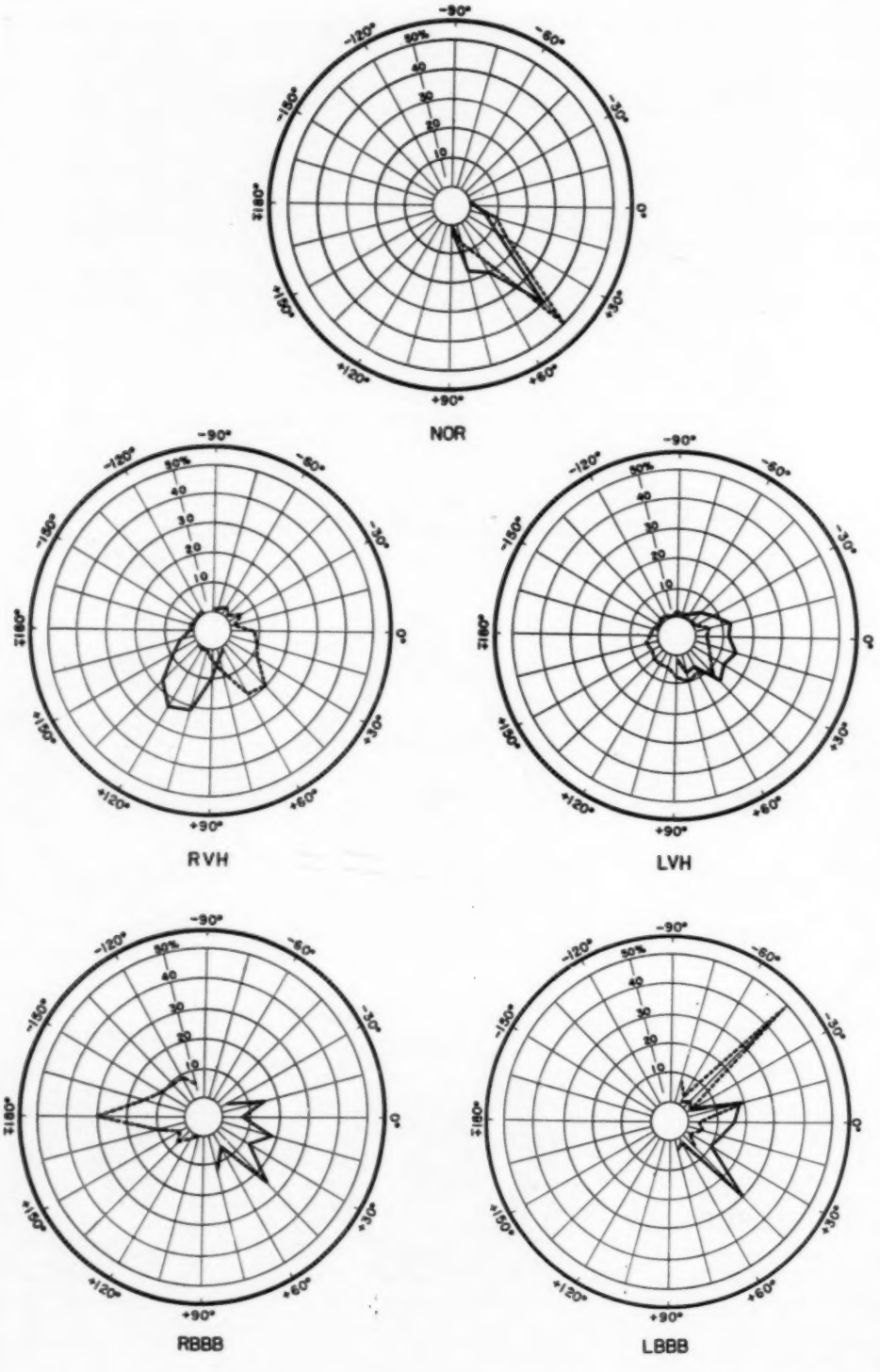


Fig. 4.—Vectorial directions of QRS and T in Normals, RVH, and LVH, and of QRS′ and QRS″ in RBBB and LBBB. The concentric circles represent percentage, from within outward, 10%, 20%, etc. Those for QRS and QRS′ are in solid curves, those for T and QRS″, in dashed curves.

By the use of this form we have studied various heart vectors in the frontal plane from thousands of electrocardiograms. This report will present data obtained from normal electrocardiograms (Normals) and from electrocardiograms of right ventricular hypertrophy (RVH), left ventricular hypertrophy (LVH), pure complete right bundle branch block (RBBB), and pure complete left bundle branch block (LBBB). These classifications were made according to the criteria established by F. N. Wilson and associates.[3] All were 12-lead records (I, II, III, aV_R, aV_L, aV_F, V_1 through V_6), taken with a direct-writing electrocardiograph.* Clinical data or post-mortem findings were not considered.

Out of about 5,000 electrocardiograms there have been included in the present series 558 of Normals, 170 of RVH, 337 of LVH, 100 of RBBB, and 50 of LBBB. In Normals, RVH, and LVH we visualized in the circular form the frontal plane QRS vector, the T vector, and the angle defined by the QRS and T vectors from each electrocardiogram; and in RBBB and LBBB, the QRS′ vector, the QRS″ vector, and the angle defined by the QRS′ and QRS″ vectors.† Fig. 3 was selected at random by way of example. In this figure the above heart vectors from limb lead electrocardiograms in *A* were visualized at a glance in the circular form in *B*.

RESULTS

The incidence in the various directions of the QRS vector and T vector in Normals, RVH, and LVH, and of the QRS′ vector and QRS″ vector in RBBB and LBBB is summarized in Table I.

In 6 electrocardiograms of RVH and 38 of LVH the T wave was either diphasic or zero potential in each limb lead; its vector could not be determined, therefore, in the RLF plane.

The incidences in percentage in the various directions of the QRS vectors and T vectors in Normals, RVH, LVH, and of the QRS′ vectors and QRS″ vectors in RBBB and LBBB are diagrammatically illustrated in Fig. 4.

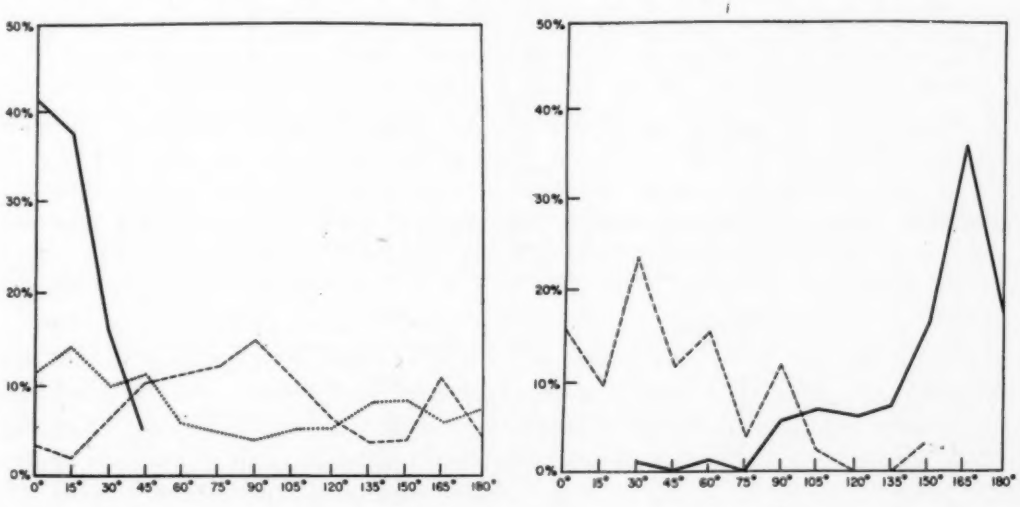


Fig. 5.—*A*, The angles formed by QRS and T vectors in Normals (solid line), in RVH (dashed line), and in LVH (dotted line). Abscissa: angles; ordinate: percentage. *B*, The angles formed by QRS′ and QRS″ vectors in RBBB (solid line) and in LBBB (dashed line). Abscissa: angles; ordinate: percentage.

*Sanborn Viso-Cardiette, Sanborn Company, Waltham, Mass.

†All vectors were area vectors of Ashman in the frontal plane. The QRS′ vector is the first main QRS vector, the QRS″ vector is the second. Only vectorial directions were concerned in this report.

The average QRS vector was directed toward +45 degrees in Normals, toward +120 degrees in RVH, and toward +15 degrees in LVH. In RBBB the average QRS′ vector was directed toward +30 degrees, the average QRS″ vector

TABLE I. NUMERICAL DATA OF QRS AND T VECTORS IN NORMALS, RVH, AND LVH; AND OF QRS′ AND QRS″ VECTORS IN RBBB AND LBBB

	NORMALS		RVH		LVH		RBBB		LBBB	
	QRS	T	QRS	T	QRS	T	QRS′	QRS″	QRS′	QRS″
0°	12	9		13	42	11	7		8	2
+15°	36	52		17	51	16	18		6	3
+30°	69	91		21	45	20	12		5	1
+45°	222	281		32	50	38	25		15	3
+60°	107	77	2	30	22	24	6		1	
+75°	97	45	7	13	24	28	13		2	
+90°	14	1	17	6	6	22				
+105°			38	1		16		1		
+120°			39	2		14				
+135°			29	1		16		6		
+150°			15			13		3		
+165°			11			14		10		
∓180°			3			8		30		
−15°	1	2		4	43	14	16		9	10
−30°				9	26	4	3		1	1
−45°				2	16	5			2	24
−60°				5	8	1			1	2
−75°				4	4	3				4
−90°				3		7				
−105°						1		6		
−120°			3			6		9		
−135°			2			6		9		
−150°			1			3		11		
−165°			3			9		15		
	558	558	170	163	337	299	100	100	50	50

TABLE II. NUMERICAL DATA OF THE ANGLES FORMED BY QRS AND T VECTORS IN NORMALS, RVH, AND LVH; AND BY QRS′ AND QRS″ VECTORS IN RBBB AND LBBB

	NORMALS	RVH	LVH	RBBB	LBBB
0°	228	5	32		8
15°	212	4	43		5
30°	91	10	30	1	12
45°	27	16	32		6
60°		18	17	1	8
75°		20	14		2
90°		25	11	6	6
105°		17	14	7	1
120°		12	16	7	
135°		6	25	8	
150°		6	25	17	2
165°		17	18	36	
180°		7	22	17	
	558	163	299	100	50

toward −165 degrees. In LBBB the average QRS′ vector was directed toward +30 degrees, the average QRS″ vector toward −30 degrees.

The findings regarding the angles formed by the QRS vector and T vector in Normals, RVH, and LVH, and by the QRS′ vector and QRS″ vector in RBBB and LBBB are summarized in Table II.

The incidence in percentage of the various angles in these electrocardiographic states is diagrammatically illustrated in Fig. 5.

In Normals the angle formed by the QRS vector and T vector did not exceed 45 degrees. In RVH and LVH this angle could range between 0 degree and 180 degrees. In RBBB the angle formed by the QRS′ vector and QRS″ vector usually exceeded 90 degrees; the average angle was 150 degrees. In LBBB the angle formed by the QRS′ vector and QRS″ vector usually did not exceed 90 degrees; the average angle was 45 degrees.

DISCUSSION

In Normals the QRS-vector and T-vector curves (Fig. 4) representing incidence in percentage in the various directions were almost identical in form and location, and they had the same maximum at +45 degrees.

It is clear that in RVH the QRS-vector curve resided at the right of the RLF plane, and the T-vector curve resided at the left of the RLF plane. In LVH the QRS-vector curve resided at the left of the RLF plane, but the T-vector curve was closed in an irregular circle.

In 6 electrocardiograms of RVH and 38 of LVH the T wave was either diphasic or of zero potential in each limb lead; its vector could not be determined in the RLF plane. This was 4 per cent in RVH and 11 per cent in LVH.

In RBBB the QRS″-vector curve resided extremely to the right in the RLF plane, and in LBBB it resided extremely to the left in the RLF plane. In both RBBB and LBBB the QRS′-vector curve resided in about the same region as that of the QRS-vector curve in Normals. Thus, in the RLF plane the general direction of activation of a single normal ventricle, either right or left, was nearly the same as that of the normal QRS vector. The route of activation of a blocked ventricle, either right or left, was abnormally altered—toward the right in RBBB, toward the left in LBBB.[4,5]

The three limb electrodes, R, L, and F, are not equidistant from each other and from the heart; the heart is not a fixed-point source of the electromotive field; and the interposed tissue between heart and electrodes is not homogeneous and not of large dimension. Therefore, the Einthoven assumption is not consistent with the reality, and the Einthoven triangle cannot give accurate results no matter how carefully it is employed.[6]

Based on the lead vector concept, the Burger triangle, on the other hand, could give accurate results in experiments, irrespective of thorax shape, heart-vector eccentricity, and tissue heterogeneity.[8-10] By the use of either of the diagrams (A or B[7]) which convert Einthoven triangle data into average "normal" Burger triangle data, we found that the average normal QRS vector at +45 degrees, as presently obtained, appeared to be more accurate than at +58 degrees, as determined by careful measurements.

SUMMARY

1. The Einthoven triangle has been set forth in the circular form. The circular form correlates easily the polarities written in the six limb leads and the corresponding heart-vector direction in the RLF plane.

2. The average QRS vector was directed toward +45 degrees in normal electrocardiograms, toward +120 degrees in right ventricular hypertrophy, and toward +15 degrees in left ventricular hypertrophy. The average QRS′ vector was directed toward +30 degrees in both complete right bundle branch block and left bundle branch block. The average QRS″ vector was directed toward −165 degrees in complete right bundle branch block, and toward −30 degrees in complete left bundle branch block.

3. In normal electrocardiograms the angle formed by the QRS vector and T vector did not exceed 45 degrees. In right ventricular hypertrophy and left ventricular hypertrophy this angle could range between 0 degree and 180 degrees. In complete right bundle branch block the angle formed by the QRS′ vector and QRS″ vector usually exceeded 90 degrees; the average angle was 150 degrees. In complete left bundle branch block the angle formed by the QRS′ vector and QRS″ vector usually did not exceed 90 degrees; the average angle was 45 degrees.

4. The incidence of complete right bundle branch block was 2 per cent, of which 95 per cent were of the Wilson type. The incidence of complete left bundle branch block was 1 per cent.

5. The T vector could not be determined in 4 per cent of right ventricular hypertrophy and in 11 per cent of left ventricular hypertrophy.

6. In the RLF plane the general direction of activation of a single normal ventricle, either right or left, was nearly the same as that of the normal QRS vector. The route of activation of a blocked ventricle, either right or left, was abnormally altered: toward the right in complete right bundle branch block, and toward the left in complete left bundle branch block.

7. The circular form was found to be advantageous in clinical routine electrocardiographic analysis.

We wish to thank Mr. George W. Newman and his staff in the Department of Medical Illustration for making the drawings, and Miss Jennie Selma Wolfer, of the Heart Station, for her valuable technical assistance.

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The Dynamics of the Left Ventricular Border in Chronic Constrictive Pericarditis: An Analytic Roentgenkymographic Study With Remarks on the "Flat Top and V" Electrokymographic Pattern

Antonello Laconi, Palermo, Italy

The kymographic study of the mechanics of the ventricles has been aided by plane roentgenkymography (Stumpf[8] and Berner[2]), but the characteristics of this method limit its usefulness to a generic evaluation of the motion of the border of the heart. In recent years several reports have appeared on the electrokymogram in chronic constrictive pericarditis.

Gillick and Reynolds[6] and, later, McKusick[7] reported that the characteristic feature of the left ventricular electrokymogram in chronic constrictive pericarditis is the pattern known as "flat top and V," which consists of a horizontal plateau with a V-shaped dip formed by the descending limb of ventricular ejection and the ascending limb of the following phase of rapid filling, the ascending stroke being the mirror image of the descending stroke. This electrokymographic pattern has been attributed to the impediment to diastolic filling caused by the rigidity of the ventricular walls.

Contro and Magri[5] studied the electrokymograms of 85 persons, of whom 20 were normal and 65 suffered from different types of heart disease. Among the tracings from these 85 persons, 16 showed the "flat top and V" pattern. Only 2 persons were found to suffer from chronic constrictive pericarditis, 12 had varying forms of heart disease, and 2 were normal. The authors concluded that this finding is not pathognomonic of constrictive pericarditis but may be encountered in other diseases of the cardiovascular system.

We report in this paper the result of a study on the dynamics of the left ventricular border in chronic constrictive pericarditis, made by means of Cignolini's analytic roentgenkymography, and compare our results with the electrokymographic findings.

MATERIAL

A group of 16 subjects with chronic constrictive pericarditis, including 12 operated upon by

From the Istituto di Radiologia Medica e Terapia Fisica dell'Università di Palermo (Direttore: Prof. P. Cignolini).
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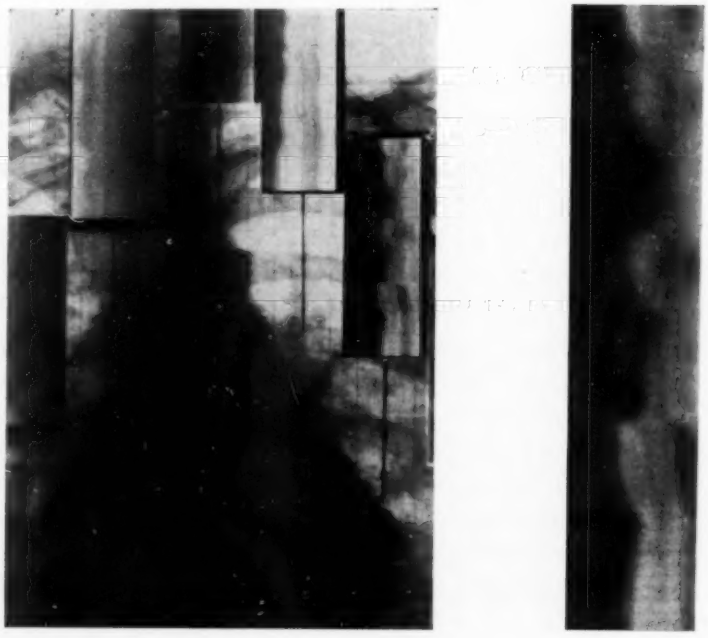
pericardiectomy, were studied by analytic roentgenkymography. The patients were examined in the anteroposterior and in the oblique projections at varying degrees of rotation.

All the operated patients were again examined by analytic roentgenkymography approximately 1 month after surgery.

RESULTS

In 9 patients the tracings on the left ventricular border showed absence of any cyclic phenomena. The kymograms showed a perfectly straight line during apnea, and some oscillations of a respiratory origin during breathing. Slight and abnormal signs of cyclic activity were found in a few instances on the lower segment of the ventricular border.



A. *B.*

Fig. 1.—Chronic constrictive pericarditis. *A*, Analytic roentgenkymograms recorded on the lower and mid-portions of the left ventricle, the pulmonary artery, the aorta, and the lower and upper arches of the right border. *B*, Analytic roentgenkymogram of the left ventricle (natural size). Note the trapezoid pattern of the tracing recorded on the left ventricle. Read from bottom to top. Speed: 1 mm. = 3 hundredths of a second.

In 4 other cases the cycles were clearly evident but their contour was greatly deformed. The tracings showed a steep lateral movement during rapid filling, and standstill during slow filling, the steepness of slope of the systolic descending limb being equal to that of the ascending limb of rapid filling. The resulting pattern had a trapezoid form, with absence of secondary components. This "trapezoid" pattern corresponds to the diastolic "flat top and V" pattern described in the electrokymogram by American authors (Figs. 1, *A*, *B*, and 2, *A*, *B*).

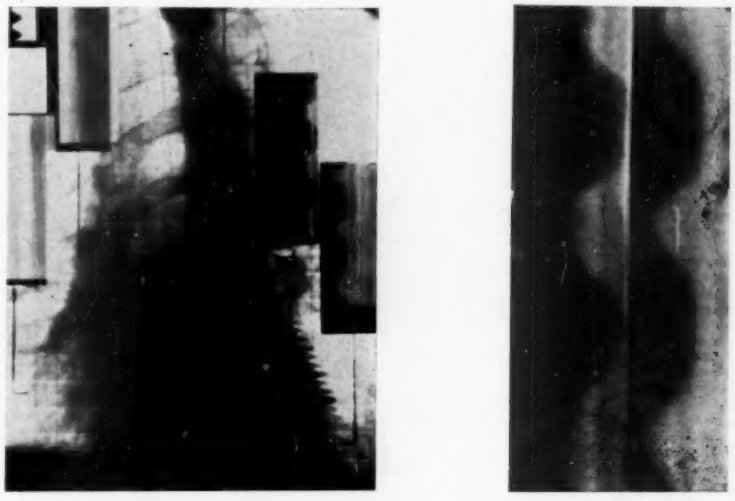
In the remaining 3 cases the ventricular kymoanalytic tracing showed a trapezoid pattern which differed from the previously described pattern only because the deflections were shorter.

COMMENT

The trapezoid pattern was found in a total of 7 cases. This pattern is never encountered in normal persons. It has been reported in other types of cardiovascular diseases.

As long ago as 1934, Cignolini[3] described a trapezoid pattern in the ventricular kymoanalytic tracings recorded in patients with mitral incompetence. Recent studies[4] on the analytic roentgenkymogram made in a group of mitral patients treated by surgery confirmed Cignolini's finding. The secondary components, however, are invariably present, to a greater or lesser degree, in the tracings of such patients. This is especially true for the *s* wave of the early ejection phase and the *r* wave of the rapid filling resulting from the passage into the ventricle of the regurgitating wave (Fig. 3, *A* and *B*).

One of our cases of atrioventricular block showed a trapezoid pattern, but this was a 12-year-old girl with mitral stenosis and incompetence, who developed an atrioventricular block. The mitral incompetence by itself may account for the finding. In this case the severe heart enlargement and the dynamics of the atrioventricular block may have contributed to the disappearance of secondary components in the ventricular kymoanalytic tracings (Fig. 4, *A* and *B*).



A. *B.*

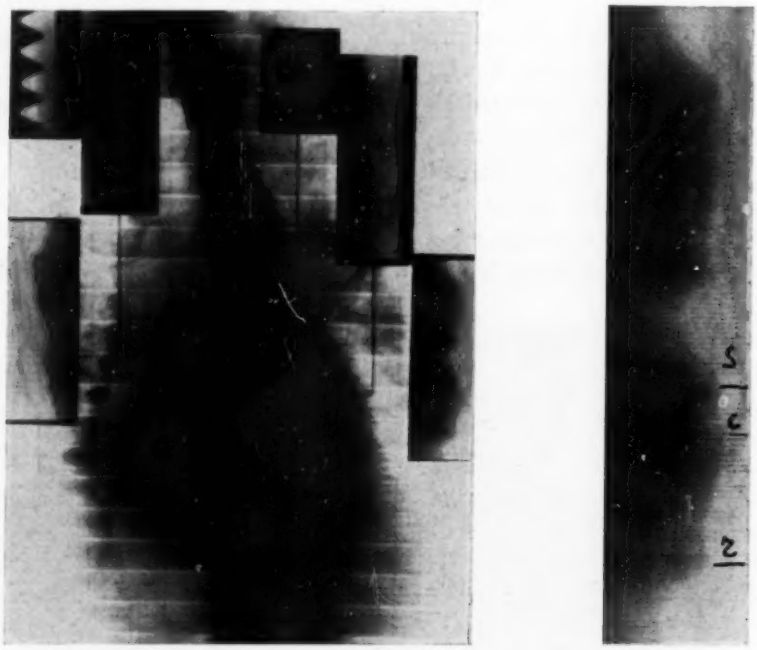
Fig. 2.—Chronic constrictive pericarditis (confirmed at surgery). *A*, Polykymograms recorded in the left anterior oblique projection. *B*, Analytic roentgenkymograms recorded on the left ventricle, lower and mid-portions (natural size): The two strips were recorded in the left anterior oblique projection. Note the trapezoid pattern of the tracing recorded on the left ventricle.

A trapezoid pattern with poorly evident secondary components was found in a few cases of heart failure with marked enlargement of the heart. In contrast with the tracings of chronic constrictive pericarditis, the straight lines and angles were not so sharply defined in such cases.

We may conclude that the trapezoid pattern of the left ventricular analytic roentgenkymogram of constrictive pericarditis shows some characteristics which distinguish it from similar pathologic tracings, and that it is never encountered

in normal persons. Hemodynamic and positional factors contribute to the genesis of the trapezoid pattern.

In regard to hemodynamic factors, the resemblance to pressure tracings from the right ventricle is very suggestive. At the onset of diastole the intraventricular pressure level is relatively low and the blood flows freely into the ventricles; soon, however, the limit of distensibility of the walls is attained, and this causes an arrest or slowing of the inflow. This phenomenon is expressed on pressure tracings by the so-called "diastolic plateau at a high pressure level" (horizontal plateau throughout diastole[1]).



A. *B.*

Fig. 3.—Mitral stenosis and incompetence (confirmed at surgery). *A*, Analytic roentgenkymograms recorded on the left ventricle, the left auricle, and the lower arch of the right border. *B*, Kymoanalytic tracing of the left ventricle (natural size), showing the trapezoid pattern that may be encountered in this condition. Note, however, the ample *r* wave at the end of rapid filling and the presence of an *s* wave; in other words, the secondary components are visible.

In regard to positional factors, the fibrous formations encasing the cardiovascular pedicle may result in a limitation or deviation in a certain direction of the torsion movements of the heart, and thus contribute to modifying the amplitude of the ventricular tracings.

The nonuniform findings obtained by electrokymography in chronic constrictive pericarditis were mentioned briefly at the beginning of this paper. According to the information gained by analytic roentgenkymography, such discordant results are to be ascribed to the conditions under which electrokymograms are recorded. At times the electrokymographic tracing is attributable almost exclusively to changes in the cardiovascular silhouette; at other times it depends to a great extent on volumetric and positional changes of the paracardiac shadows,

so that the ventricular cycle is either obliterated or radically deformed. For the sake of brevity we will omit discussion of other factors which may alter the electrokymogram (unequal sensitivity of the photocell, inverse relation between amplitude of the tracing and rate of registration, variations due to tension and amperage, difficulty of obtaining exact chronologic values).

In conclusion, it is likely that the lack of universal agreement on the diastolic "flat top and V" pattern described by Gillick, Reynolds and McKusick is due to the characteristics of the electrokymographic technique. In a large percentage of cases the analytic roentgenkymogram shows the trapezoid pattern which corresponds to the "flat top and V" pattern. The greater uniformity of the results obtained by analytic roentgenkymography is due to the greater fidelity of registration of the morphologic, chronologic, and quantitative factors which this procedure permits.

A. *B.*

Fig. 4.—Mitral stenosis and incompetence complicated by atrioventricular block. *A*, Analytic roentgenkymograms recorded on the mid-portion of the left ventricle, the left middle arch, and the right lower arch. *B*, Kymoanalytic tracing (natural size) showing the trapezoid pattern of the left ventricle.

SUMMARY

The "flat top and V" pattern of the electrokymogram in chronic constrictive pericarditis is discussed, as well as the different opinions expressed by the various authors in regard to this finding. The findings obtained by analytic roentgenkymography in 16 cases of chronic constrictive pericarditis are reported. Such findings may be classified into two main types: a first type, which consists of a straight line due to standstill of the ventricular border, and a second type, trapezoid in form, due to partial rigidity of the walls. It is suggested that the discrepancies in the electrokymographic findings may be explained by the kymo-

analytic results with two reasons: (1) The trapezoid pattern is not constant but only statistically prevalent. (2) Even in cases having a trapezoid type of movement, the electrokymogram may be deformed by variations in density of the paracardiac shadows.

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Electrocardiogram in Chronic Severe Anemia

L. M. Sanghvi, M.R.C.P. (London), D.T.M. & H. (England), S. N. Misra, M.D., K. Bannerji, M.B.B.S., and K. D. Gupta, M.D., Jaipur, India

Electrocardiographic abnormalities in chronic anemia have been variously reported either to be of no significance[1] or to have a high incidence[2-5]; to disappear with relief of anemia[6] or to persist[4,7]; and to be proportionate to the severity of anemia[8] or to show no correlation.[5] They have been attributed to ischemia of the myocardium,[9,10] subendocardial necrosis,[11] increased vagal tone,[12] and, in sickle cell anemia, to myocardial scarring[10] or coronary occlusion.[13,14] A complete study of the abnormalities and their eventual course during and after recovery from anemia is possible only in curable anemias when serial tracings can be obtained until the anemia is cured and thereafter. The purpose of this paper is to report the results of such a study in 100 patients with chronic severe anemia.

MATERIAL AND METHODS

One hundred patients, 63 males and 37 females, with anemia of at least 3 months' duration, hemoglobin values of 8 Gm. per 100 ml. or less, and no other cardiovascular disease were selected. All patients were hospitalized until the anemia was cured. Their ages ranged from 8 to 50 years, with an average of 26 years. Hemoglobin at the time of admission varied from 2 to 8 Gm., with an average of 3.6 Gm. Anemia was due to chronic malaria in 50 patients, ancylostomiasis in 20, bleeding hemorrhoids in 5, chronic dysentery in 10, and uterine bleeding in 6, and was of an unknown etiology in 9 patients. Duration of the anemia varied from 3 months to 5 years, with an average of 13 months. The cardiothoracic ratio varied from 41 to 89 per cent, and cardiac enlargement was present in 78 patients. Heart failure was present in 30 patients, 11 of whom were females.

Serial electrocardiograms with standard leads, I, II, III, and unipolar leads, aV_R, aV_L, aV_F, and V_{1-6}, were obtained from the time of admission until the anemia was completely cured, and for a further period of 2 to 6 months in many of the patients showing persistence of abnormality. The electrocardiogram was considered abnormal if the alterations were definite or if serial tracings confirmed them. Minor changes in the amplitude of the QRS complex and the T waves were not considered as definite abnormalities. A P-R interval of more than 0.20 second and a Q-T ratio of more than 1.09 in males and 1.08 in females were considered abnormally prolonged.[15] Left ventricular hypertrophy pattern was determined by the criteria of Sokolow and Lyon.[16] Teleroentgenograms of the chest were obtained on admission and after the anemia was cured. The heart was considered enlarged if the cardiothoracic ratio was 50 per cent or more, or if subsequent examination revealed reduction in size.

From the Department of Cardiology, Sawai Man Singh Hospital and Medical College, Jaipur, India.

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RESULTS

Electrocardiographic Findings.—A normal electrocardiogram was obtained in 15 cases at the time of admission, and in none of these did any abnormality appear in subsequent tracings. Abnormalities in 85 cases are summarized in Table I.

The cardiac rate varied from 50 to 125 per minute, with sinus tachycardia in 49 cases and sinus bradycardia in 9 cases, except in 1 case with tachycardia. The latter appeared to be atrial in origin since the P waves in Leads II and III were upright (Fig. 1). Atrial premature beats in 1 case caused a bigeminy. Ventricular premature beats in 2 cases were due to parasystole often causing fusion beats

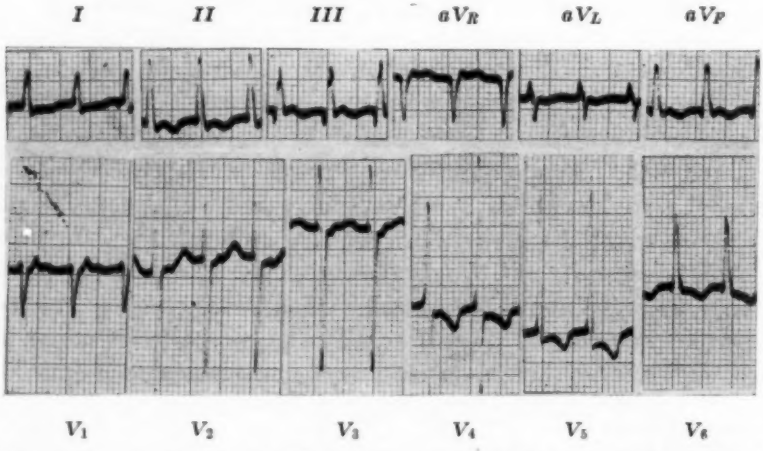

Fig. 1.—Electrocardiogram of a 32-year-old woman, showing atrial tachycardia, P-R interval of 0.26 second, and S-T and T changes with left ventricular hypertrophy and strain pattern.

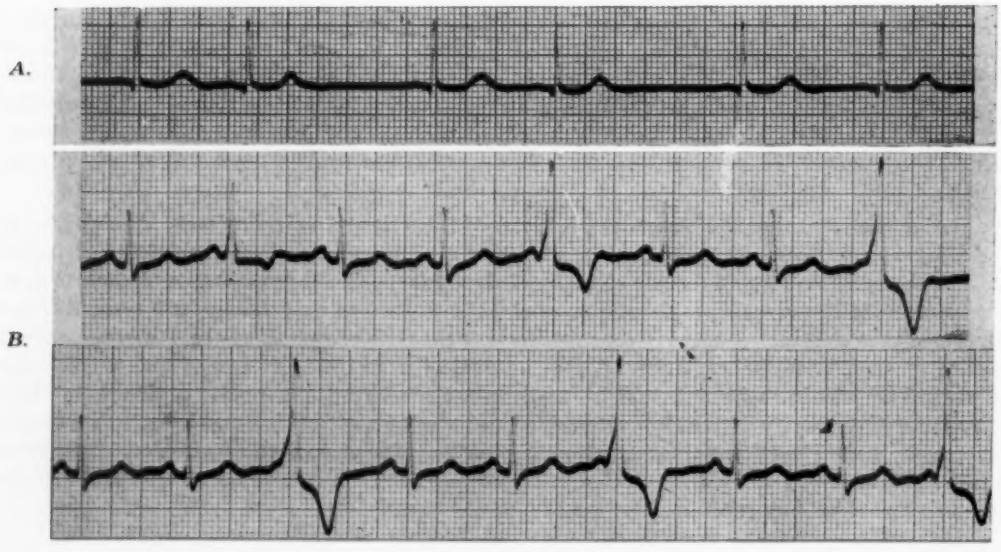

Fig. 2.—Electrocardiograms showing atrial premature beats causing a bigeminal rhythm (*A*), and ventricular premature beats and fusion complexes due to parasystole (*B*). The two strips in *B* are continuous records.

(Fig. 2). P changes, flattening or inversion, were always associated with some other abnormality in the electrocardiogram. Significant changes in the amplitude of the QRS complex were due to appearance or regression of a left ventricular hypertrophy pattern, except in a case with congestive failure in which an abnormally low amplitude was due to pericardial effusion.

S-T depression was seen in 54 cases, most frequently in Leads II, III, aV_F, and V_{4-6}. In 10 of these the electrocardiogram rapidly became normal when the hemoglobin level rose to 7 Gm. Despite improvement of anemia, the S-T depression in 12 cases was followed by inverted T waves in the same precordial leads, and in 5 cases a left ventricular hypertrophy pattern, and in 8 cases a strain pattern, developed (Fig. 3).

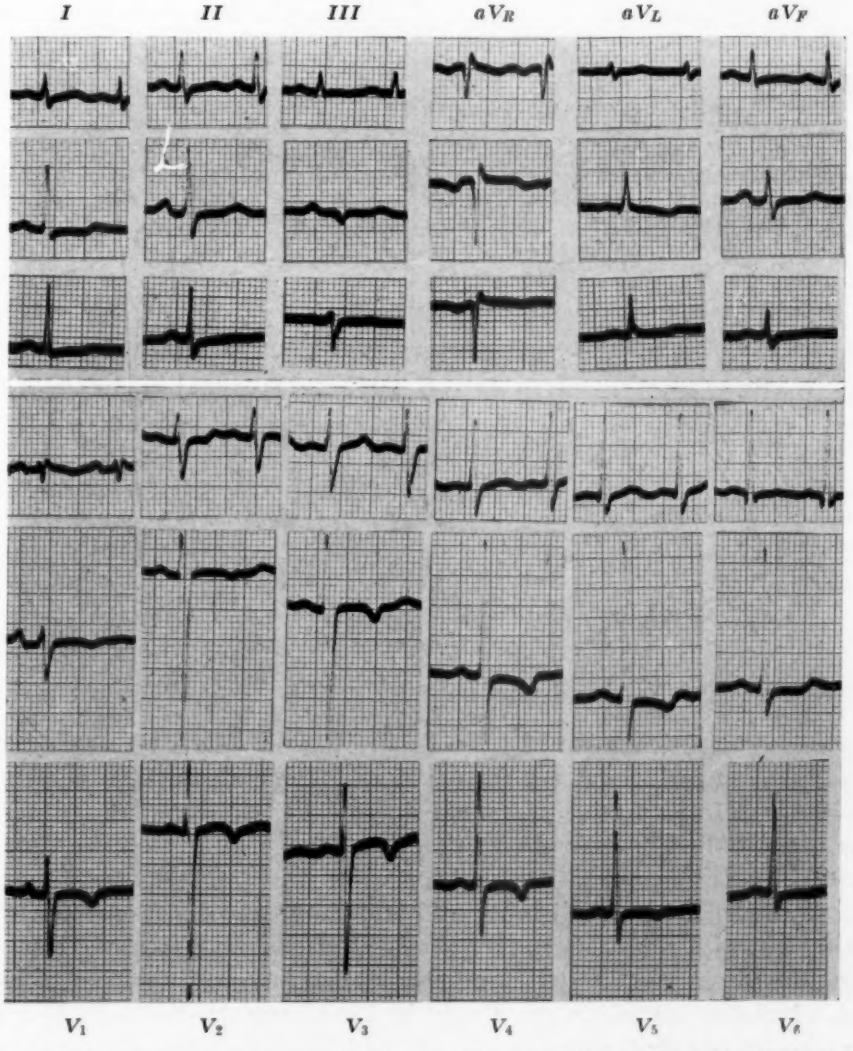

Fig. 3.—Serial tracings of a 17-year-old girl. *A*, Feb. 28, 1957. Hemoglobin 3 Gm. S-T segment depression in Leads aV_L and V_{2-6}. *B*, April 6, 1957. Hemoglobin 9 Gm. T waves have become inverted in Leads aV_L, and V_{1-5}, and left ventricular hypertrophy and strain patterns have appeared. *C*, June 15, 1957, 6 weeks after cure of anemia, persistence of S-T and T changes and left ventricular strain pattern.

Inversion of T waves was seen in 62 cases, most frequently in Leads III, aV_L, and V_{1-3}, and was associated with S-T changes in 44 cases. Two cases showed isolated T-wave negativity in precordial Leads V_{3-4} (Fig. 4). T changes usually took a long time to regress with improvement of the anemia; in some cases they regressed only after cure of the anemia. Inverted T waves in 3 of the 10 cases in which thiamine was administered intravenously in 100 mg. doses, daily for 1 week, became upright, again to become inverted within 3 to 7 days (Fig. 5).

TABLE I. INCIDENCE OF ELECTROCARDIOGRAPHIC ABNORMALITIES IN 85 CASES, AND PERSISTENCE OF ABNORMALITIES AFTER CURE OF ANEMIA IN 36 CASES

ABNORMALITIES	NUMBER OF CASES	NUMBER OF CASES WITH PERSISTENCE
P changes	24	—
ST-T changes	72	27
U changes	2	—
Q-T interval prolonged	18	4
P-R interval prolonged	4	2
Left ventricular hypertrophy	15	13
Left ventricular strain	13	10
Atrial premature beats	6	—
Ventricular premature beats	5	1
Atrial tachycardia	1	—
Hypopotassemia	1	—

TABLE II. AGE DISTRIBUTION OF 100 CASES, AND OF 36 CASES WITH PERSISTENT ABNORMALITIES

AGE (YR.)	TOTAL CASES	NUMBER OF CASES WITH PERSISTENCE
0–10	3	1
11–20	29	11
21–30	39	15
31–40	17	3
41–50	12	6

Both cases with inversion of U waves in precordial Leads V_{2-4} (Fig. 4) had heart failure and considerable cardiac enlargement, the cardiothoracic ratio being 66 and 76 per cent, respectively. Of the 4 cases with prolonged P-R interval, in 1 it was associated with a paroxysm of atrial tachycardia, becoming normal after cessation of the paroxysm, and was probably the result of temporary myocardial fatigue. In another instance it appeared after improvement of the anemia. In the 2 cases in which this abnormality persisted after cure of the anemia, administration of atropine, gr. 1/100 intravenously, caused no alteration of the P-R interval. Hypopotassemic pattern seen in 1 case was due to electrolyte imbalance as a result of severe diarrhea.

Persistence of abnormalities (Table I) despite cure of anemia was seen in 36 cases, and was found to have no relation to the age of the patient (Table II). Twenty-eight of these cases had persistent cardiac enlargement.

Correlation of Abnormalities With Other Factors.—Abnormalities were more frequent in the female patients, being present in 34 out of the 37. There was no relation to the etiological factor and the duration of anemia. The incidence and the nature of the abnormalities seemed to be closely related to the hemoglobin

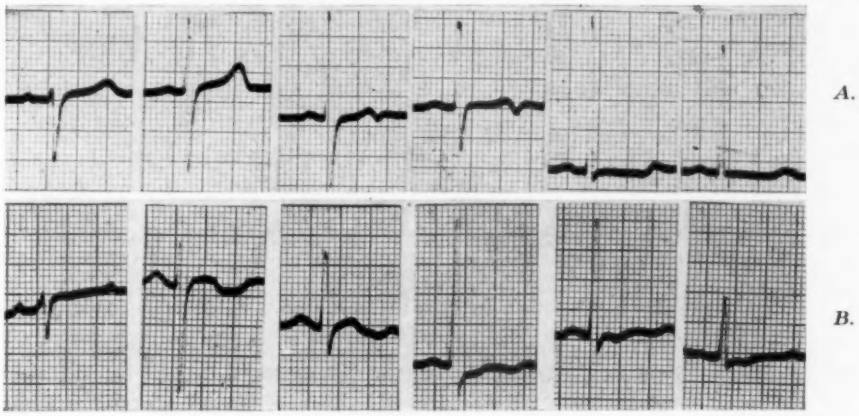

Fig. 4.—Electrocardiograms showing isolated negativity of (*A*) the T waves in Leads V_{3-4}, and (*B*) the U waves in Leads V_{2-4}.

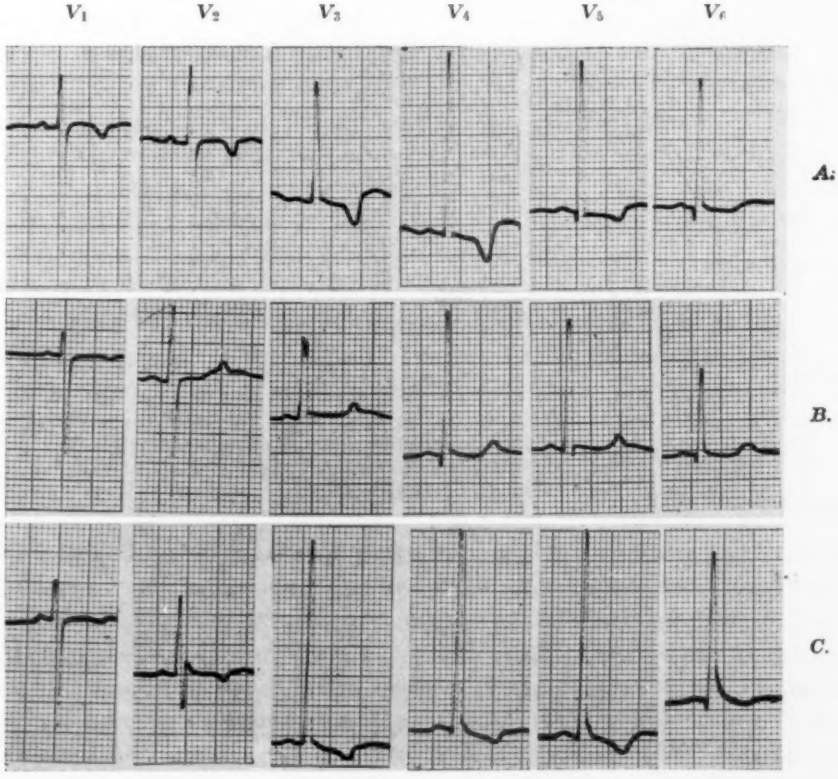

Fig. 5.—Electrocardiograms showing effect of thiamine. *A*, Sharply inverted T waves in Leads V_{1-5} on admission. *B*, After 7 injections of thiamine, T waves are now upright in Leads V_{2-5}. *C*, The T waves are again sharply inverted, 4 days after *B*.

level and the cardiac size on admission (Table III). The hemoglobin level was less than 5 Gm., and the cardiothoracic ratio was more than 55 per cent in most of the cases with U changes, prolonged P-R and Q-T intervals, and left ventricular hypertrophy or strain pattern. Abnormalities were present in every case with a cardiothoracic ratio of 60 per cent or more. Absence of a constant relation was evident, however, because normal electrocardiograms were obtained in 4 cases with less than 3 Gm. hemoglobin and in 8 cases with cardiac enlargement, while 7 cases with more than 7 Gm. hemoglobin and 15 cases without cardiac enlargement showed abnormal tracings. A left ventricular hypertrophy pattern was seen in 3 instances in the absence of any cardiac enlargement. In all of the 30 cases with heart failure, an abnormal electrocardiogram was obtained. Q-T changes were seen in 12 (40 per cent), and persistence of abnormalities in 15 (50 per cent), of the 30 cases with failure, while these were seen, respectively, in 5 (7 per cent) and 21 (30 per cent) of the 70 cases without failure.

TABLE III. INCIDENCE OF CASES WITH ABNORMAL ELECTROCARDIOGRAMS, AND SOME OF THE ABNORMALITIES ACCORDING TO THE HEMOGLOBIN LEVEL AND CARDIAC SIZE ON ADMISSION

	TOTAL CASES	NUMBER WITH ABNORMALITIES	ABNORMALITY (NUMBER WITH)			
			L.V.H.	L.V.S.	Q-T PROLONGED	P-R PROLONGED
Hemoglobin (Gm./100 ml.)						
Up to 3	49	45 (92%)	5	11	15	4
3–5	30	27 (90%)	8	2	2	–
5–8	21	13 (62%)	2	—	—	–
Cardiac size and C-T ratio (%)						
No enlargement	22	15 (68%)	3	—	—	–
Up to 55	37	30 (81%)	3	2	4	–
55–60	14	13 (93%)	3	3	1	1
Above 60	27	27 (100%)	6	8	12	3
Total	100	85	15	13	17	4

L.V.H. and L.V.S. = left ventricular hypertrophy and strain, respectively.

DISCUSSION

Eighty-five per cent incidence of electrocardiographic abnormalities in this series is higher than in any reported previously and is probably due to the greater intensity of the anemia. Many of the abnormalities observed have been described by other authors. But, isolated T-wave and U-wave negativity in precordial leads, parasystole, atrial bigeminy, atrial tachycardia, and S-T depression changing to inversion of T waves have not been reported previously. Right axis deviation[8] and tall notched or peaked P waves[2,8,12] reported in sickle cell anemia were not seen in a single instance.

The incidence and the nature of the abnormalities showed a fairly close, though not a constant, relation to the severity of the anemia and the cardiac

size. A high incidence of left ventricular hypertrophy and strain patterns was noteworthy, the latter pattern in anemia having been reported by only one other writer.[2] Left ventricular hypertrophy pattern was seen with comparatively higher hemoglobin levels and less cardiac enlargement than the strain pattern. It was present in 3 cases on admission and in 5 cases after cure of the anemia, in the absence of cardiac enlargement. This is understandable because hypertrophy may not be detectable roentgenologically. In patients with congestive heart failure, the electrocardiogram was abnormal in every instance, and the incidence of Q-T changes and persistence of abnormalities was high. Hookworms have been reported to have a toxic action on the myocardium,[17] but there was no difference in this series in the incidence of abnormalities in cases with anemia due to hookworm infestation and anemia due to other causes. A higher incidence of abnormalities in the female patients appeared to be due to the comparatively larger cardiac size encountered in them than in the males.

An interesting feature revealed in this study was that several cases showed an increase of the abnormalities after improvement or even cure of the anemia. This suggests that myocardial scarring, hypertrophy, and consequent relative ischemia and strain may become manifest in the electrocardiogram only when the initial cardiac dilatation disappears with improvement of the anemia. Of particular interest was the appearance of left ventricular strain pattern in 8 cases after cure of the anemia. This shows that increased vascularity of the myocardium reported to occur in anemia[18] may not be sufficient for the hypertrophied musculature. Again, in some cases, despite improvement of anemia, deeply inverted T waves appeared in the precordial leads which had earlier shown S-T segment depression. The inverted T waves then generally became upright after a period of 3 to 16 weeks. It appears that these changes might be due to coronary insufficiency leading to a subendocardial zone of myocardial infarction with an overlying region of transmural myocardial ischemia.[19]

Another interesting feature was the persistence of abnormalities despite cure of the anemia in as many as 36 cases. Unfortunately all of them could not be followed up, but in 18 of them, who have been followed for a period of from 2 to 6 months after cure of the anemia, the abnormalities have not regressed. In sickle cell anemia, persistence has been attributed to myocardial scarring due to blockage of arterioles by sickled erythrocytes.[10] Such a possibility does not exist in the anemias in this study. In other cases persistence is believed to be due to concomitant coronary sclerosis.[11] In the present series, 26 of the 36 patients with persistent abnormalities were below 30 years of age, 1 of them being an 8-year-old boy, and there was no significant difference in the incidence in patients over 40 years of age. Its incidence was higher in the female patients in whom coronary sclerosis is uncommon except in the presence of diabetes or hypertension. It was associated with persistent cardiac enlargement in a majority of the cases. There seemed, therefore, little doubt that coronary sclerosis had little to do with persistence of abnormalities and that the latter was caused by persistent and probably irreversible cardiac changes as a result of prolonged hypoxemia. It is realized, however, that in some of these cases the abnormalities may regress in the course of time.

The influence of thiamine on T waves in 3 cases was unusual. None of the 3 patients had any clinical evidence of deficiency. Inverted T waves due to myocardial damage and nutritional deficiency could not have become upright, only to be reinverted again. It may be that in chronic anemia there is an abnormal myocardial thiamine metabolism, as has been noted in acute posthemorrhagic anemia.[20]

The mechanisms of production of the abnormalities appeared to be several: (1) temporary coronary insufficiency without cardiac damage in cases with S-T segment depression which rapidly became normal with slight improvement of anemia; (2) subendocardial infarction and reversible cardiac changes in those in whom the abnormalities regressed very slowly, in some only after the cure of the anemia; (3) persistent and probably irreversible cardiac changes in cases with fixed abnormalities; (4) congestive failure per se; (5) temporary myocardial fatigue due to tachycardia causing transient prolongation of the P-R interval; (6) electrolyte imbalance as a result of diarrhea causing a hypopotassemic pattern; and (7) probably abnormal myocardial thiamine metabolism. Increased vagal tone was not responsible for the prolonged P-R interval in the case in which this abnormality persisted.

The diagnosis of the presence of rheumatic or other types of heart disease in patients with severe anemia has been a problem. During the 2-year period of this study, 3 such cases were encountered. The electrocardiograms were of no help in any of them. It is felt, therefore, that in the absence of definite clinical evidence, the presence of coincidental heart disease in such cases cannot be established until after the anemia has improved or is cured. Diastolic murmurs in curable anemias disappear rapidly with improvement of anemia,[3] and their persistence should immediately arouse suspicion of a coincidental heart disease.

Dr. L. R. Sarin, Superintendent, Sawai Man Singh Hospital, kindly permitted the publication of this report.

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The Circulation in Hyperthyroidism: A Cardiac Catheterization Study Before and After Treatment

S. Humerfelt, M.D., O. Müller, M.D., and O. Storstein, M.D.,** Bergen, Norway*

In hyperthyroidism the heart and circulation are influenced in two different ways. First, the increased body metabolism will impose an extra load on the heart, as in prolonged muscular work. In the long run the heart muscle will hypertrophy and, in severe cases, eventually fail. Secondly, the thyroid hormone may disturb the normal cardiac rhythm, producing paroxysmal or persistent auricular fibrillation, with detrimental effect on the circulation.[11] The thyroid hormone may also adversely affect the heart muscle itself by increasing the wear and tear on the cells through the locally increased metabolism.[12]

It was shown in 1924, by Davies and associates[1] and by Liljestrand and coworkers,[2] in 1925, that the increase in "basal" metabolic rate resulting from the increased requirement and consumption of oxygen by the tissues causes an increase in the cardiac output. These investigators also demonstrated that the oxygen utilization of the tissues did not increase with increase in metabolic rate, for the arteriovenous oxygen difference diminished. The increased metabolic rate found in normal subjects during exercise also leads to an increase in cardiac output, but, here, increase in the arteriovenous oxygen difference does occur.

An increase in cardiac output may be met by tachycardia, increase in stroke volume, or a combination of both factors as is the case in normal subjects during muscular work.

According to most investigators, the stroke volume shows, on the whole, little change in thyrotoxicosis, and is an unimportant factor in the augmentation of the cardiac output. Thus, in 1932, Boas[4] demonstrated that the percentage increase of heart rate in thyrotoxicosis, measured during sleep, corresponded closely to the increase both in basal metabolism and cardiac output, whereas Fullerton and Harrop,[5] in 1930, found an increase in stroke volume as well as in heart rate.

Several authors[1,2,5] have demonstrated a decrease in cardiac output following thyroidectomy, by using the foreign gas methods of Krogh-Lindhart or Marshall and Grollman.

From the Department of Medicine, Bergen University Clinic, Bergen, Norway.
Received for publication Feb. 20, 1958.
*Present address: The University Institute for Respiratory Physiology, Ullevaal Sykehus, Oslo, Norway.
**Present address: Nordland County Hospital, Bodö, Norway.

There are some reports on the cardiac output in thyrotoxicosis determined by the direct Fick principle during cardiac catheterization,[7] but there are, to our knowledge, few reports on the changes in cardiac output after therapy has been completed.

This report concerns the influence of thyrotoxicosis on the circulation, studied by means of cardiac catheterization before and after treatment with antithyroid drugs.

MATERIAL

A total of 32 patients, 11 males and 21 females, were investigated. Of these, 9 males and 6 females were recatheterized after treatment. The average age was 39½ years. The age distribution of the men was fairly even, in contrast to that of the women which showed one peak between 25 and 29 years and another between 40 and 49 years.

The treatment given was methyl- or propylthiouracil until the basal metabolic rate fell to about +25 to +15 per cent, followed by local x-ray therapy (250 r. daily, a total of 2,250 r.).

Symptoms.—The duration of symptoms averaged 2½ years (males 1½ years, and females 2¾ years) and varied from a quarter of a year to 20 years. Enlargement of the thyroid gland was found in 29 of the 32 patients. Exophthalmos was found in 17 patients, being particularly marked in 3 patients. In 2 of the patients subtotal thyroidectomy had been performed, but the symptoms were still marked.

Thyrotoxic auricular fibrillation was found in 5 patients on admission (Cases 5, 8, 21, 29, and 32). One patient (Case 3) had had a patent ductus arteriosus ligated 3 years previously and was now free from cardiac symptoms. The venous pressure was normal in all patients.

No patient showed signs of anemia, and none had diastolic hypertension.

Except for the 5 patients mentioned, all had normal sinus rhythm, and no other ECG changes were noticed.

The average heart volume on x-ray was 352 ml. per square meter of body surface, calculated from Jonsell's formula. Two female patients had definitely enlarged hearts (Cases 5 and 21), and slight enlargement was found in one male patient (Case 32).

The average basal metabolic rate on admission was +58 per cent. At the time of the first cardiac catheterization it was +55 per cent, and by the second it had fallen to an average of +15 per cent.

METHODS

Cardiac catheterization was performed in the conventional way with pressure recordings from the pulmonary artery, right ventricle, and right auricle. The sternal angle was chosen as the zero point.

The arteriovenous oxygen difference was calculated from manometric oxygen determinations of blood sampled from the pulmonary artery, or from the right ventricle and a peripheral artery. Oxygen consumption was determined by means of a Krogh spirometer or Douglas bag, and cardiac output was estimated according to the direct Fick principle.

RESULTS

Before Treatment.—The average cardiac output before treatment was 10.4 L. per minute, with variations from 6.0 to 19.3 L. per minute. The average cardiac index of all cases was 6.1 L. per minute per square meter of body surface for both men and women. In 14 normal subjects investigated by one of the present authors[8] by the same methods, an average index of 4.5 ± 0.52 L. per minute per square meter of body surface was found. Thus, an average increase in basal metabolic rate of 55 per cent was observed to be accompanied by an average increase in cardiac output of 61 per cent.

Myers and associates[7] studied 14 patients with thyrotoxicosis and observed an average increase in cardiac index of 72 per cent as compared to that in 15 normal subjects, concomitant with a rise in basal metabolic rate of 54 per cent. E. S. Brannon (cited by Myers[7]) observed an increase in cardiac index of 68 per cent, together with a basal metabolic rate of +72 per cent.

The average increase in cardiac output relative to the increase in basal metabolic rate in our patients, therefore, seems to lie between that observed by Myers and that observed by E. S. Brannon.

The cardiac output in our patients, however, showed higher numerical values than were observed in the two investigations cited. The average cardiac index in the 15 normal subjects studied by Myers was 3.97 ± 0.17 L. per minute per square meter of body surface.

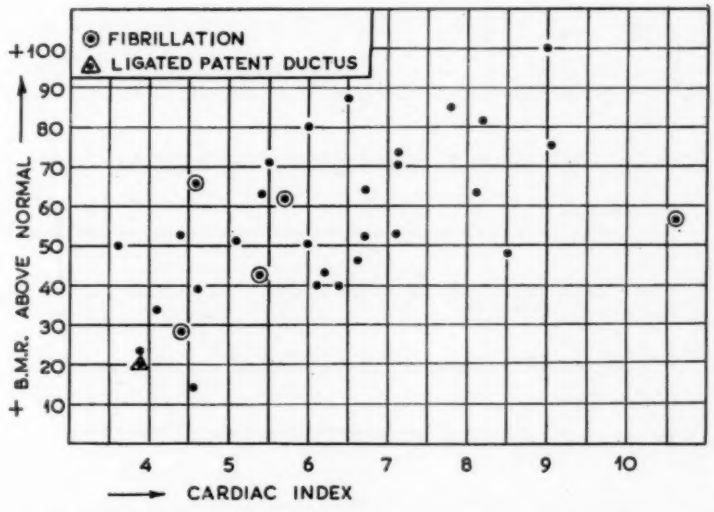

Fig. 1.—Cardiac index in relation to basal metabolism before treatment.

Fig. 1 illustrates the relationship between basal metabolic rate and cardiac index before treatment. It shows that increasing metabolic rate leads to higher cardiac output, but with some scatter (the correlation coefficient r = 0.77). Four of the patients with auricular fibrillation showed a lower cardiac index (4.0 L. per minute per square meter of body surface) than the average, while the last patient with auricular fibrillation had a strikingly high cardiac output, the arteriovenous oxygen difference being remarkably small (experimental error ?). The correlation coefficient between basal metabolic rate and cardiac index when the patients with auricular fibrillation are omitted is 0.85. This reduces the residual variance in cardiac index to 28 per cent of the basic variance.

The arteriovenous oxygen difference showed no distinct deviation from the normal observed by Storstein.[8]

The heart rate averaged 105 per minute, varying from 84 to 124 per minute.

The stroke volume showed an average value of 58.3 ± 2 ml. per square meter of body surface, with variations from 87 to 38 ml. These findings agree well with the results of Myers (54 ± 3 ml.) and those of E. S. Brannon (58 ± 4 ml.).

TABLE I. CARDIAC CATHETERIZATION BEFORE TREATMENT

CASE	BASAL METABOLIC RATE (%)	A-V O_2 DIFF. (ML./L.)	STROKE VOLUME (ML./M.^{2})	CARDIAC INDEX	PRESSURE RECORDINGS (MM. Hg)						
					PULMONARY ARTERY			RIGHT VENTRICLE			RIGHT AURICLE (MEAN)
					SYSTOLIC	DIASTOLIC	MEAN	SYSTOLIC	DIASTOLIC	MEAN	
1	+53	47.9	56	4.4				30	0	11	
2	71	44.1	57	5.5						8	
3	20	39.9	44	3.9						11	
4	87	38.6	65	6.5	23	3	15	32	−2	10	−3
5	43	33.0	56	5.4				33	0	13	2.5
6	51	42.2	47	5.1	30	10		30		8	−3
7	85	31.2	65	7.8				28	0	14	
8	66	45.9	52	4.6	30	10	18	38	−4	12	1
9	14	32.7	43	4.6	25	8	17	29	−1	12	0
10	63	39.9	54	5.4							0
11	53	29.7	59	7.1	24	10	18	24	−3	6	−2
12	34	39.8	45	4.1	24	5	11	26	−2	8	3
13	59	33.9	67	6.7	25	3	12	37	−5	9	−2.5
14	39	40.5	43	4.6	24	3	12	26	−3	11	−3
15	52	28.2	60	6.7	24	6	10	28	−3	7	−3
16	40	30.5	57	6.0	25	4	8	28	−1	14	−2
17	81	27.9	87	8.4	25	8	15	31	−4	11	0
18	50	50.0	38	3.6							−1
19	80	33.3	50	6.0	28	14	19	30	−2	14	0
20	50	30.6	56	6.0	25	6	10	27	−2	6	−4
21	62	33.3	67	5.7	35	7	20	35	−4	6	
22	71	26.9	68	8.5	25	6	11	30	−6		−5
23	63	28.7	67	8.1	27	11	14	31	−3	9	−3
24	40	32.4	57	6.4	26	6	14	28	−1	8	2
25	47	28.9	57	6.6	22	2	6	22	−3		−2
26	00	25.1	75	9.0	30	6	13	32	−3	8	−3
27	70	25.2	65	7.1	23	4	12	24	−2	3	
28	23	36.5	47	3.9							
29	57	15.2	85	10.6	27	6	12	27			
30	43	33.5	57	6.2	27	2	8	31	−1	6	0
31	73	25.9	67	7.1	23	8	12	23	−2	8	−3
32	28	36.0	52	4.4	21	4	8	22	−5	4	−5
	$\bar{x}$ +55 σ 21.9	$\bar{x}$ 33.98 σ 7.45	$\bar{x}$ 58.3 σ 11.3	$\bar{x}$ 6.13 σ 1.63	$\bar{x}$ 25.75 σ 3.06	$\bar{x}$ 6.33 σ 3.01	$\bar{x}$ 12.83 σ 3.7	$\bar{x}$ 28.74 σ 3.76	$\bar{x}$ 2.48 σ 1.57	$\bar{x}$ 9.12 σ 2.98	$\bar{x}$ −1.6 σ 2.1

Pressure recordings are listed in Table I. The average systolic pressure in the pulmonary artery was 25.75 mm. Hg, the diastolic pressure 6.33 mm. Hg, and the mean pressure 12.83 mm. Hg, while the average systolic pressure in the right ventricle was 28.74 mm. Hg. These readings are all definitely elevated when compared to those of Storstein's control subjects.[8] They are, however, 4 to 7 mm. Hg lower than the pressures observed by Myers.[7] The difference seems in part, or altogether, to be accounted for by the different zero-levels employed.

After Treatment.—Recatheterization (Table II) was performed immediately before discharge, after the antithyroid therapy had shown satisfactory effect and before the patients were adjusted to the maintenance dosage. During this period of treatment the metabolic rate fell to an average of +15 per cent.

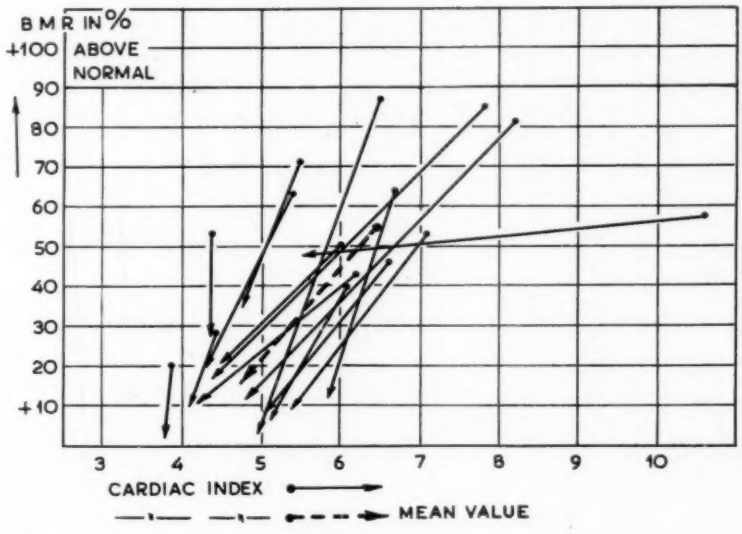

Fig. 2.—Cardiac index in relation to basal metabolic rate before and after treatment.

The cardiac output, calculated as cardiac index, showed a clear and significant decrease to an average of 4.67 L. per minute per square meter. This is only slightly higher than the normal value found by Storstein.[8] The difference between the cardiac index before and after treatment, 2.45 L. per minute, was significant to 1 per cent. Fig. 2 shows how the cardiac index tended toward the normal range, and the mean values for the cardiac index converged on the normal value of 4.5 L. per minute[8] after treatment.

The arteriovenous oxygen difference showed only a slight and insignificant fall after treatment, from 33.98 to 32.05 ml./L.

In addition, the average stroke volume showed only an insignificant fall from 58.3 to 55.6 ml. per square meter after treatment. However, in the patients with the highest cardiac outputs before treatment, a decrease in stroke volume was observed. Thus, of 6 patients with a cardiac index of more than 6.5 before treatment, a fall in stroke volume was recorded in 5, while all 3 patients with a cardiac index of more than 7.5 showed a fall. A decrease in stroke volume was

TABLE II. CARDIAC CATHETERIZATION AFTER TREATMENT

CASE	BASAL METABOLIC RATE (%)	A-V O_2 DIFF. (ML./L.)	STROKE VOLUME (ML./M.^{2})	CARDIAC INDEX	PRESSURE RECORDINGS (MM. Hg)						
					PULMONARY ARTERY			RIGHT VENTRICLE			RIGHT AURICLE (MEAN)
					SYSTOLIC	DIASTOLIC	MEAN	SYSTOLIC	DIASTOLIC	MEAN	
1	+27	33.7	54	4.4				25			
2	35	40.2	48	4.8				22	−2	8	0
3	1	36.4	44	3.8				22	−5	7	
4	3	30.6	61	5.0	21	9	15	28	−1	12	0
7	17	35.8	58	4.4	30	7	12	28	−1	8	0
10	19	36.7	51	4.3	17	5	8	23	−1	8	−2
11	9	27.7	67	5.4	14	8	13	16	−2	8	−5
13	12	29.2	64	5.8	17	7	13	27	−1	11	
15	1				24	8	10	24	+1	10	
16	6	27.4	50	4.5							
17	12	29.5	60	4.3	17	4	9	22	0	6	0
20	24	31.7	47	4.5							
25	6	24.0	25	5.0				22	−2	8	−2
29	48	28.2	65	5.5							−2
30	11	35.4	55	4.2	22	7	10	23	−2	8	1
32	10	34.2	55	4.1	19	6	11				−2
	+15 σ 8.07	$\bar{x}$ 32.05 σ 4.6	$\bar{x}$ 55.6 σ 6.66	$\bar{x}$ 4.67 σ 0.52	$\bar{x}$ 20.1 σ 5.07	$\bar{x}$ 6.8	$\bar{x}$ 11.2	$\bar{x}$ 23.5 σ 3.19	$\bar{x}$ 1.6	$\bar{x}$ 8.5	$\bar{x}$ 1.3

also observed in all 4 patients with a reduction in cardiac index of more than 2.0 L. per minute per square meter of body surface.

The pulse rate decreased during treatment from an average of 105 to 85 per minute, which is a significant fall. The change in pulse rate is therefore (in most cases) the decisive factor in the decrease in cardiac output after treatment. In the most pronounced cases, however, a decrease in stroke volume also takes place initially.

Pressure Recordings.—A decrease was found in the systolic pressure in the pulmonary artery as well as in the ventricle. The decrease in the systolic pressure in the right ventricle averaged 5.2 mm. Hg and was significant to 0.1 per cent. The diastolic pressure in the pulmonary artery showed a small increase; thus a distinct fall in pulse pressure was obtained. The mean pulmonary artery pressure was practically unchanged, as was the right auricular pressure (Fig. 3).

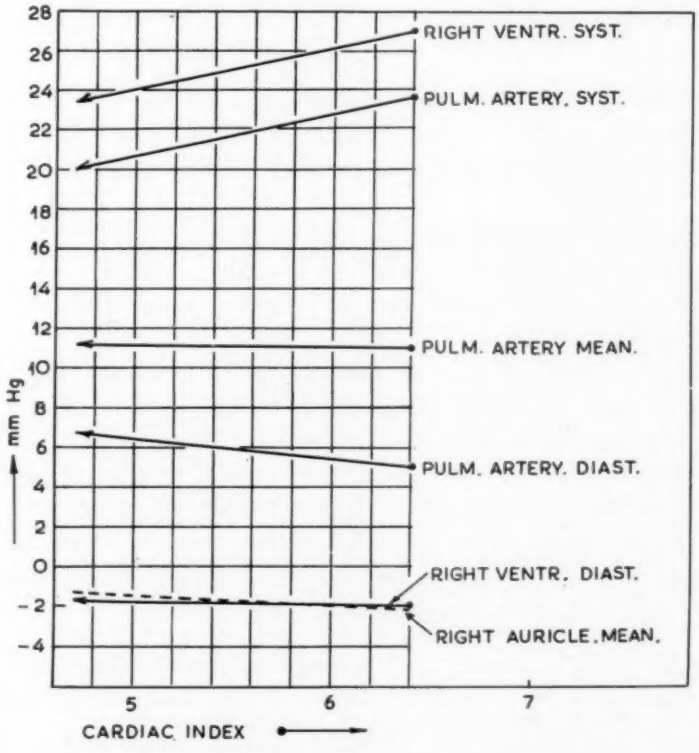

Fig. 3.—Pressure recordings in relation to cardiac index, before and after treatment. Mean values.

The systolic pressures in the pulmonary artery and right ventricle were still somewhat increased compared to those in normal subjects.[8] The metabolic rate in these patients, however, was not completely normal.

Parallel to the decrease in pulse pressure and systolic pressure in the lesser circulation were similar changes in the systemic circulation. The average systolic pressure fell from 150 to 117 mm. Hg, and the pulse pressure declined from 72 to 50 mm. Hg.

CONCLUSIONS

1. This investigation confirms that increase in cardiac output in hyperthyroidism is practically paralleled by increase in heart rate. The demonstrated reduction in the cardiac output resulting from treatment with antithyroid drugs is followed by a similar reduction in heart rate. Changes in stroke volume and arteriovenous oxygen difference play no significant part in most cases. However, in those cases with a very high cardiac output a decrease in stroke volume may occur after treatment.

2. The increased cardiac output in hyperthyroidism is accompanied by an elevation of the systolic pressure in the right ventricle and pulmonary artery, with an increase in pulmonary artery pulse pressure.

3. Effective treatment leads to a reduction in cardiac output, together with a decrease in the systolic pressure and the pulse pressure in the pulmonary and systemic circulations.

SUMMARY

The influence of increased body metabolism on the circulation has been studied by means of cardiac catheterization in 32 patients with thyrotoxicosis. In 15 patients recatheterization was performed after treatment with antithyroid drugs.

The average cardiac index before treatment was 6.1 ± 1.63 L. per minute per square meter of body surface, with an average increase in basal metabolic rate of 55 per cent. After treatment the cardiac index showed a significant decrease to an average of 4.67.

The pulse rate decreased significantly during treatment; the arteriovenous oxygen difference and the stroke volume showed only a slight fall. Only in the patients with the highest cardiac outputs before treatment and the greatest fall during treatment was a marked reduction in stroke volume observed.

The increased cardiac output in hyperthyroidism is accompanied by an elevation of systolic pressure in the pulmonary artery and the right ventricle. Effective treatment leads to a decrease in systolic pressure and pulse pressure in the pulmonary, as well as in the systemic, circulation.

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Ballistocardiographic Findings on the J Wave

George Bodrogi, M.D., Budapest, Hungary

As is well known, a characteristic double murmur is originated in cases in which there is a temporal deviation in the function of the two ventricles, and in which a preliminary condition for the origin of a murmur is present. This double murmur can be remarkably well observed on phonocardiograms.

Fallot's tetralogy gives the best example of this double murmur. The right ventricle contracts considerably later than the left one, and such a great temporal displacement permits the separate auscultatory observation of the two murmurs and the identification of the murmurs on the phonocardiogram. This same asynchronism is proved also by the accelerated ballistocardiogram (BCG). The graphs made with the BCG measuring and recording the acceleration* frequently show a distinct double J wave with almost totally equal peaks, and the distance between the two phenomena attains 0.10 second.

In some verified cases of Fallot's tetralogy repeated ballistocardiograms have been taken showing synchronously each time three sounds and a venous or an aortic curve. After thorough examination we realized that two high waves were appearing and almost covering the entire systole as double J waves, which confirms our conviction that this double J is incident to the duality of the rapid ejection. That is to say that the first J wave corresponds to the left ventricle's ejection phase, the second to that of the right ventricle. This opinion is supported by the observation that on the phonocardiogram the pulmonary closing may be well seen. The oscillation of the closing of the aorta is also visible on the logarithmic and high-frequency lead and preceding the pulmonary closing (see Fig. 1).

Double J waves, however, may be found elsewhere, also, as in auricular septal defect and pulmonary stenosis. In the case of auricular septal defect (see Fig. 2) the distance between the double J was 0.08 second, corresponding to the asynchrony between the two ventricles. This same may cause the duplicated first and second sounds also.

From the School of Welfare, Center for Heart Diseases, Budapest, Hungary (Director: Alexander Plenczner, M.D.)

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*The apparatus on principle described by Ueda and Tsui was constructed by Bodrogi, Hajdu, Plenczner, and Szepessy.

Fig. 3 shows the mechanogram of a patient suffering from pulmonary stenosis. The double J wave with a difference of 0.10 second can be well observed also.

Double J waves may also be found quite frequently in distinct cases of mitral stenosis of high degree. In one of our cases the interval between the double J peaks is 0.07 second. Sound and venous graphs show clearly that in this case

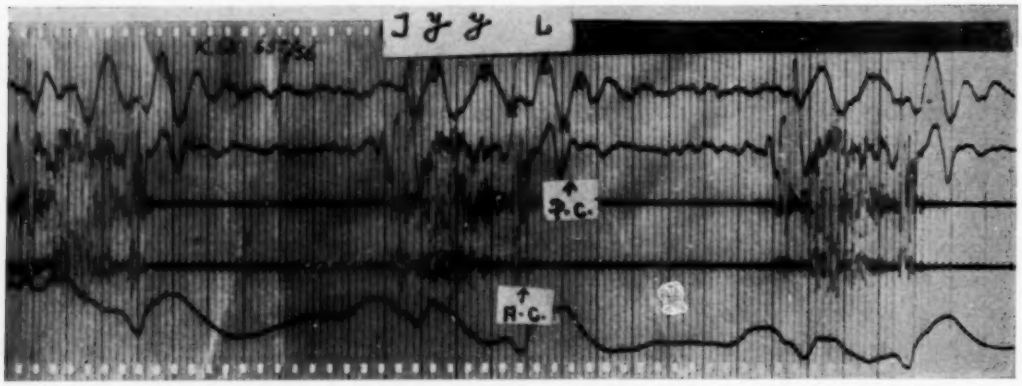

Fig. 1.—Ballistocardiogram, phonocardiogram, and venous curve. *A.C.* = aortic closing. *P.C.* = pulmonary closing.

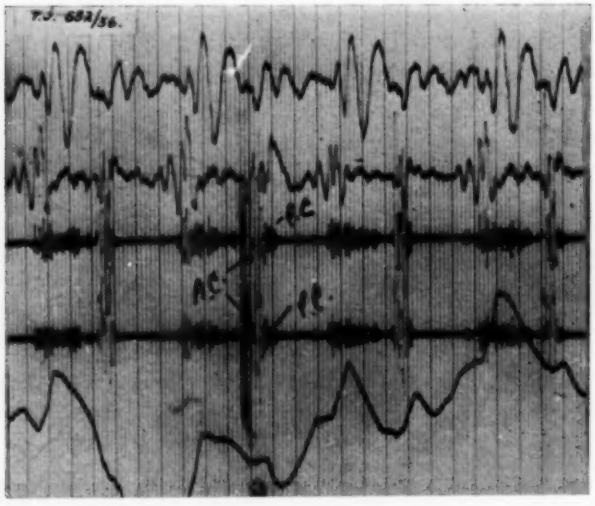

Fig. 2.—The distance between the double J is 0.08 second, corresponding to the asynchrony between the two ventricles.

the closing of the aortic valve precedes the pulmonary closing. These two phenomena explain, therefore, that the two ventricles are functioning asynchronously, the right one lagging behind by 0.07 second. In each of the above cases a great strain on the right heart has existed. There can be no doubt that with such a strain on the right heart the action of the right ventricle may be delayed,

i. e., certain phases may be periodically postponed. It is also known that the I-J phase on the BCG corresponds to the phase of rapid ejection. As we pointed out before in the cases already mentioned, a great ventricular asynchrony can be seen, and therefore the double J wave may be explained as a registered sign of double rapid ejection.

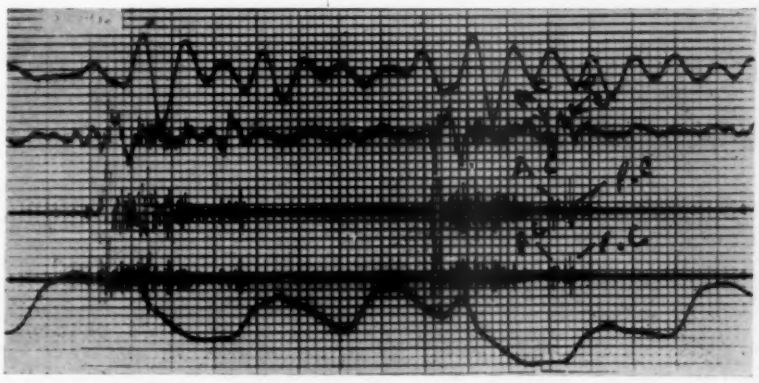

Fig. 3.—See text.

The correctness of our opinion is also supported by the fact that sound records taken from an adequate place and in a suitable manner show double first and second sounds. In Fig. 3 the closing of the aortic valve can be clearly distinguished from the pulmonary closing. The time between the two semilunar closings is approximately equal to the time between the two J waves.

In conclusion, it may be stated that the well-specified double J wave signifies the asynchrony of action of the two ventricles. Such leads may be encountered in Fallot's tetralogy, auricular septal defects, and pulmonary stenosis.

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High-Frequency Features in the Vectorcardiogram

H. Karni, M.D., Stockholm, Sweden

Since some authors have proved that high-frequency (HF) details appear in the depolarization phase in physiologic, and especially in pathophysiologic, conditions, this topic has gained considerable interest.

Troublesome obstacles are encountered, however, in the recording of high frequencies with the electrocardiograph of ordinary design. Even when the amplifier is capable of response to a higher frequency range without serious distortion of the curve, the mass of the tracing instrument will offer invincible difficulties. But when an amplifier of adequate design is equipped with a cathode-ray oscillograph, the chances of registering high-frequency features are much more favorable, even electrocardiographically, provided the time scale is considerably expanded.

Gilford[1] stated that a frequency response of 200 c.p.s. would be necessary in ordinary commercial electrocardiographs in order to obtain a real spectrum of frequencies without any undue distortion of the curve.

Kerwin[4] proved that the high-frequency potentials of depolarization can be satisfactorily recorded by electrocardiographic means if the apparatus responds to frequencies as high as 200 c.p.s. or more, and if a cathode-ray oscillograph is used as the recording instrument. In his interesting investigations with a cathode-ray electrocardiograph, frequency responses were selected as follows: 50, 100, 200, and 6,400 c.p.s. The paper speed was 25, 100, 250, and 500 mm. per second. In his opinion frequency responses of 50 and 100 c.p.s. are not sufficiently high, because many details are excluded from the curves. He recommends, especially for research purposes, a frequency response as high as 6,400 c.p.s. But from the curves published in his article, a comparison between 200 and 6,400 c.p.s. frequencies revealed no notable differences. It is indeed doubtful whether a frequency response as high as 6,400 c.p.s. is really required in the investigation of the heart currents. However, an upper limit of 1,000 c.p.s. seems to be very desirable, and a cathode-ray tube should naturally be used as the recording instrument.

Langner[5] reported that there were high-frequency details in his series of 21 cases of clinically treated myocardial infarctions. Only one patient did not

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From the Medical Department, Karolinska Hospital, Stockholm, Sweden (Physician-in-chief: Professor Henrik Lagerlöf).

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reveal such features. None of the 60 controls showed any similar changes when checked by means of a high-fidelity amplifier with a frequency range up to 1,000 c.p.s. and registered by a cathode-ray oscillograph. These details could not be recorded by an electrocardiograph of ordinary design.

As concerns vectorcardiography, Kerwin considers a high-frequency response desirable also in this mode of potential recording.

In the vectorial tracing of the flow of current during a single cardiac cycle the potential variations as time function will provide the shape, size, and finest contour of the VCG loop. Those delicate details in the contour of the QRSsÊ loop which appear as bending, notching, or undulatory characteristics are due to rapidly changing variations in amplitude of the HF potentials. These rapid oscillations will be accentuated in the vectorcardiogram, where the potentials are traced as resultant of xy-components. In the electrocardiograph, potentials are recorded as vertical deflections only. Those potentials which are decreasingly parallel with the lead axis will be projected as zero when they are at right angles to the axis. Consequently, the sensitivity of the electrocardiographic tracer toward the potentials with successively decreasing projection on the lead axis will decrease in direct proportion to the amount of projection. Such potentials will influence the QRS complex by time delay corresponding to the duration of these potentials with "inadequate" projection angle. Therefore, vectorcardiography seems to afford a more convenient mode of HF recording. For this reason, and because there is no need of an expanded time scale in the vectorial tracing, a comparative study seemed to be warranted in order to clarify the selectivity of the vectorcardiogram in regard to HF changes and the influence of these changes upon the conventional electrocardiogram.

MATERIAL AND METHODS

Sixty-one clinical cases were examined electro- and vectorcardiographically. The distribution of the cases showing HF details can be seen in Table I.

TABLE I. DISTRIBUTION OF THE CASES SHOWING HF DETAILS

DIAGNOSIS	NUMBER OF CASES
Myocardial infarction	2 (12)
Myocarditis, myopericarditis	3 (8)
Hypertrophy of the left ventricle	10 (41)
Total	15 (61) = 24%

Figures in parentheses designate number of cases examined in each group.

As comparative normal material, vectorcardiograms were used from 50 normal cases, 24 males and 26 females, ranging in age from 18 to 69 years. Normally, the pathway of the QRS-vector head is, almost without exception, smooth. Now and then, however, single notchings can be seen in the QRSsÊ loop; these are due to sudden changes in the direction of inscription. Neither these nor the rough impressions in the loop are considered as HF changes.

The ECG curves were taken with a Mingograph*. Its frequency range curve is essentially flat up to 600 c.p.s. The jet of ink traces the curve on the paper, the speed of which is 40 mm. per second. Unless special precautions were taken, the photographic recording of the ECG curves from the cathode-ray screen when using an expanded time scale proved to be attended by considerable difficulties. On this account the method was considered of no practical value and, therefore, was omitted from the present study.

The technical data of the 4-channel vectorcardiograph used in the present investigation have been given earlier.[2]

The amplification was 1 mv. = 3 cm. on both axes. Projections were taken on frontal (F), sagittal (S), and horizontal (H) planes according to the method described earlier.[3]

The roentgenologic heart volume was estimated according to the method introduced by Lysholm.[6,7] Normal values lie between 250 and 450 ml. per square meter of body surface.

RESULTS

A. *Myocardial Infarction.*—As can be seen from Table I, there were HF details in 2 of 12 cases of myocardial infarction. Owing to the frequent and rather marked impressions and variations in the direction of rotation of the QRSsÊ loop in this condition, the figure must be considered low. The following case will illustrate the HF features of undulatory character in myocardial infarction combined with marked enlargement of the heart.

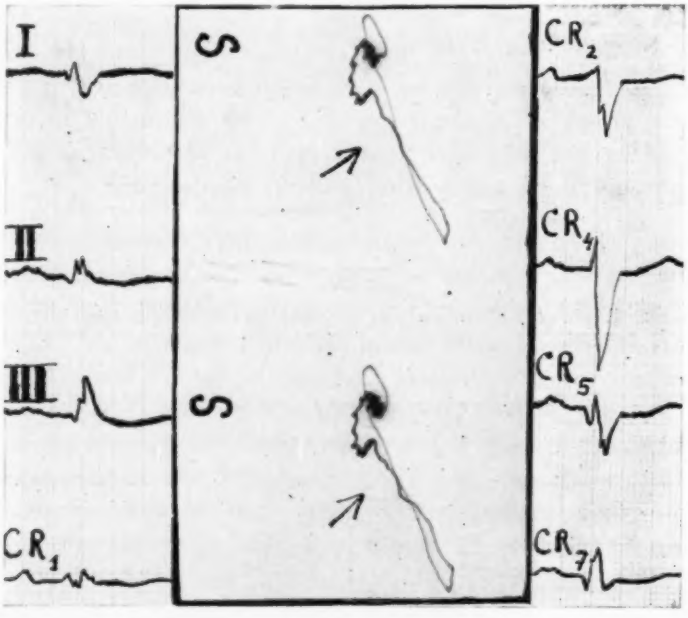

Fig. 1.—Two sagittal plane projections in a case of myocardial infarction combined with heart enlargement (roentgenologic heart volume approximately 800 ml./M.² of body surface). High-frequency oscillations are visible near the zero point in the afferent limb of the QRSsÊ loop. In each cycle they were repetitive as to localization and appearance. Small peaks at regular intervals in the TsÊ loop, giving this loop a rough appearance, are due to alternating current of 50 c.p.s. Owing to the much higher velocity of the current during the inscription of the QRSsÊ loop, the above-mentioned HF oscillations represent a considerably higher periodicity. As a matter of fact, no HF details in the TsÊ loop are ever observed. The electrocardiograms show splits in the QRS complex, which are due to directional changes of the QRS-vector head and are not produced by HF oscillations.

*A direct-writing electrocardiograph manufactured by Elema, Stockholm, Sweden.

CASE 1.—A 65-year-old railway worker with his first episode of myocardial infarction showed a classical clinical picture. After the acute period of 3 weeks, during which the patient was severely ill with attacks of shock, grave symptoms of chronic cardiac decompensation developed. The ECG did not show typical signs, but despite this the case was interpreted as myocardial infarction.

A VCG taken 3 days after the onset showed phase difference in the TsÊ loop, causing its broad appearance. Examination 6 days later showed, in addition, notchings of undulatory character in a strictly localized section near the zero point in the afferent limb of the QRSsÊ loop. The sagittal plane projection revealed this pattern best (Fig. 1). This phenomenon showed a consistently repetitive feature and did not change its character or localization from one heart cycle to another. Three months later, when the clinical picture was characterized by a grave decompensation of the left ventricle, the HF pattern was still recognizable. The heart volume showed marked increase and measured approximately 800 ml./M.^{2} of body surface, i.e., nearly 300 ml. more than 8 months earlier.

Another case with HF pattern in the QRSsÊ loop was encountered in a 69-year-old male patient with a heart volume of 480 ml./M.^{2} of body surface. This patient had had his episode of infarction 15 years previously. Also in this case there was a consistently repetitive pattern in the HF vibrations. In none of the other cases of myocardial infarction were HF details established.

B. *Myocarditis and/or Myopericarditis.*—Of the 8 cases assigned to this category there were 3 with marked HF details in the QRSsÊ loop. The following case is representative of the HF pattern in myocarditis.

CASE 2.—A 39-year-old man with repeated tonsillitis in childhood and adolescence, and with a 6 months' history of cardiac decompensation, was admitted to the Medical Department of the Serafimer Hospital because of dyspnea, precordial pain, and edema in the ankles. In the 24 hours before admission the condition had rapidly deteriorated. He developed cough and severe attacks of orthopnea. During this time the peripheral edema increased markedly. Except for fever, 38.4°C., there were neither hematological, serologic nor bacteriologic signs of infection. Nevertheless, the case was considered to represent an infectious etiology. The ECG revealed a LBBB (Fig. 2). The heart volume was 780 ml./M.^{2} of body surface. It decreased to 720 ml. after 24 days of treatment with penicillin and digitalis. At the time of the patient's discharge from the hospital the dyspnea, edema, and fever had disappeared.

The VCG showed a total discordance between the axes of the QRSsÊ and TsÊ loops. The axis of the QRSsÊ loop showed an almost anteroposterior direction. There was no pathologic phase difference recognizable in the TsÊ loop. The afferent limb of the QRSsÊ loop was markedly deformed, owing to regularly repetitive undulations of HF character. This pattern appeared in each heart cycle in the same part of the QRSsÊ loop and could be seen clearly from the S-plane projections (Fig. 2).

One of the three cases with HF details was a 27-year-old mechanic who had developed cardiac complications during the course of a typical rheumatic fever. ECG findings were left axis deviation and defective intraventricular conduction in the left ventricle. There were notchings and splits in R_{II}, S_{II}, and S_{III}. The heart volume was 380 ml./M.^{2} of body surface. The vectorcardiogram, which was at a slight angle to the frontal plane, showed sudden directional changes in the rotation of the QRS-vector head. The contour of the F-plane projection of the QRSsÊ loop was almost that of a square. There were many notchings, giving a rough appearance to the QRSsÊ loop.

The third case also showed a rheumatic etiology. A 35-year-old male patient who had suffered from pains in different joints for many years, fell acutely ill with a fever of 38.2° C. and dyspnea. The electrocardiogram showed elevation of the S-T level in Leads I and V_{5-6} and an isoelectric T wave in Leads I, II, and V_{5-6}. The heart volume measured 735 ml./M.^{2} of body surface. A myopericarditis was considered possible. The VCG was rough in appearance, with HF details of undulatory character in the middle part of the QRSsÊ loop. These findings were persistent long after the acute phase. Not until 3 years later had these HF changes disappeared. The heart volume had decreased during this time to 410 ml./M.^{2} of body surface, and the ECG was normal, also.

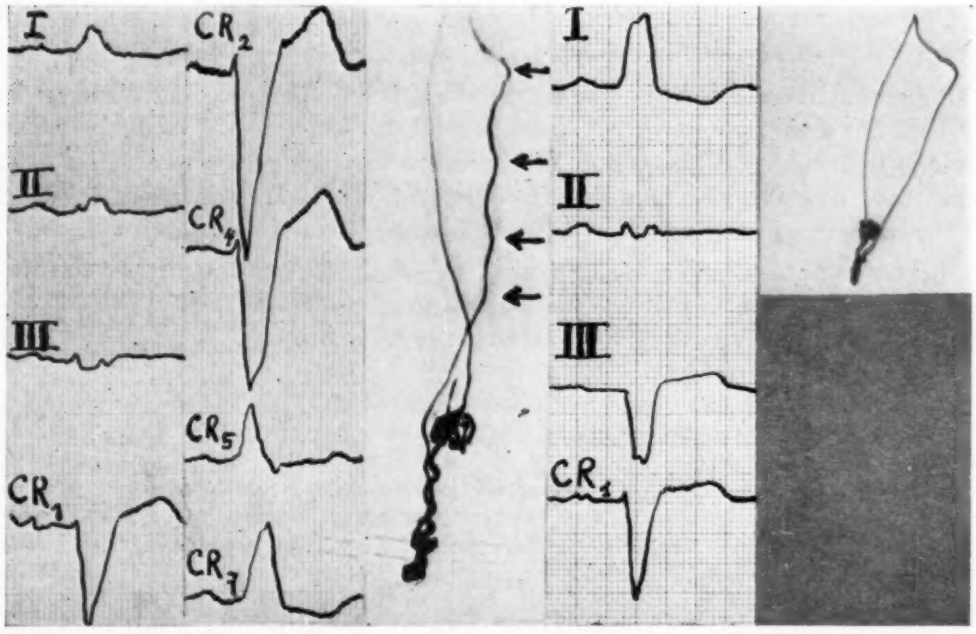

Fig. 2.—HF oscillations of undulatory character in the afferent limb of the QRSsÊ loop. Sagittal plane projections in a case of myocarditis with considerable heart enlargement (780 ml./M.^{2} of body surface) and decompensation. The electrocardiograms show a pattern of LBBB due to the delayed intraventricular conduction. A real LBBB (right) shows a rather similar electrocardiographic pattern, although there are no HF details in the QRSsÊ loop, which is of angular shape because of sudden change in the direction of the current and a late separate activation of the left ventricular wall. Thus, the flow of current in a real BBB is paroxysmal and does not necessarily show any HF details. The electrocardiographic pattern in BBB and in intraventricular conduction disturbance is similar in both conditions, giving rise to delayed QRS time. Sometimes it is possible to recognize vectorcardiographically the real reason for the delayed QRS time and to distinguish the intraventricular conduction disturbance from BBB.

C. *Hypertrophy of the Left Ventricle.*—Of 41 cases with left ventricular hypertrophy there were HF changes in the QRSsÊ loop in 10. These patients, representing a variety of clinical conditions, were examined roentgenologically, electro- and vectorcardiographically. The distribution of the cases may be seen in Table II.

The average age of these patients was 66 years, that of the entire series, 61 years. The figures for roentgenologic heart volumes were 540 and 590 ml./M.^{2},

respectively. Inasmuch as ages and heart volumes covered a fairly wide range, neither of these factors was considered to have any causative significance, although there seemed to be a tendency for HF details to appear in combination with marked enlargement of the heart. Of special interest is the following case of WPW syndrome.

CASE 3.—A male engineer, 49 years of age, had suffered from attacks of tachycardia for 20 years. The ECG showed pre-excitation and a slight depression of the S-T level in Lead I, and S-T elevation in Leads II and III (Fig. 3). The heart volume was 450 ml./M.^{2} of body surface, and the blood pressure was 115/80 mm. Hg.

In the VCG, apart from the phase difference of repolarization potentials recognizable from the broad TsÊ loop of all three plane projections, there was a strictly localized HF pattern immediately after the zero point at the beginning of the efferent limb of the QRSsÊ loop. This part of the loop was convex. It started in the posterior direction, then turned anteriorly, and continued abruptly as a smooth curve downward and to the left (Fig. 3).

TABLE II. HF PATTERN COMBINED WITH LEFT VENTRICULAR HYPERTROPHY

CASE	SEX	AGE (YR.)	BLOOD PRESSURE (MM. Hg)	HEART VOLUME (ML./M.^{2}B.S.)	ELECTROCARDIOGRAM
1.	M	69	125/65	460	Normal
2.	F	81	115/65	480	Atrial fibrillation. Left axis deviation. QRS 0.10 sec. Notchings. T wave in Leads I, II, V_{5-6} inverted
3.	M	70	125/70	470	Atrial fibrillation
4.	M	72	130/80	490	Normal
5.	F	51	170/100	500	Splits in QRS in Leads II-III. S-T depression in Leads I, V_{1-5}. T negative in Leads I-III, V_{5-7}
6.	M	69	130/80	480	Q in Leads II-III. Splits in QRS. T in Leads II-III negative, in V_5 diphasic, in V_7 negative
7.	F	72	185/90	880	Atrial fibrillation. Defective intraventricular conduction in the left ventricle. S-T depressed in Leads I, II, V_{5-7}
8.	M	69	160/80	540	RBBB
9.	M	60	205/130-115	690	S-T depressed in Leads I-III, V_{4-7}. Atrial fibrillation
10.	M	49	115/90	450	WPW syndrome. Left axis deviation. S-T depressed in Lead I

DISCUSSION

The foregoing examples illustrate the accuracy with which the HF details can be recorded vectorially, provided the technical data of the amplifiers are adequate. In the apparatus used in the present study the frequency range curve was essentially flat up to 1,000 c.p.s., which seems to be sufficient for this purpose. Owing to the lack of dependability of an expanded time scale, the present mode of HF recording is the method of choice. The high, sweeping speed, which is unfortunately necessary for revealing the HF details in ECG curves, renders photographic recording from the cathode-ray screen a troublesome process. But this is not the only reason for preferring vectorcardiographic recording. The phase difference that manifests itself in vectorial recording accentuates the response to HF changes. In electrocardiography, in which potential variations between

two points are registered linearly, HF details cannot be traced with sufficient selectivity because of their repetitive departures from the vertical deflection of the electrocardiographic tracer. Moreover, the tracer will erroneously register the potentials of this character as time delay. HF details will therefore often cause retardation, which increases the duration of the QRS complex. Hence, in the case of WPW syndrome, which showed HF changes in a strictly localized section at the beginning of the QRSsÊ loop, there was a corresponding delay in the ECG, causing the typical delta wave. The localized character of HF pattern

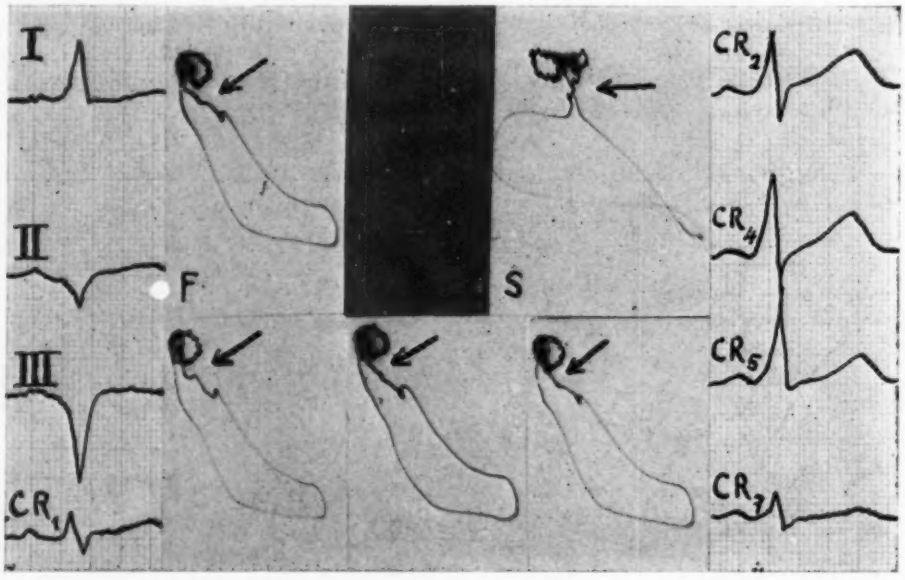

Fig. 3.—Electrocardiograms and four frontal (*F*) and one sagittal (*S*) plane projections from a case of WPW syndrome. The small arrows indicate HF features in the beginning of the QRSsÊ loop. These details show a consistently repetitive pattern in all projections. As can be seen from the sagittal plane projection, the QRS-vector head turns in the anterior direction after the inscription of the HF-patterned section. These HF oscillations cause time delay of the QRS complex, giving rise to the typical delta wave seen in pre-excitation. Neither the HF pattern nor the exact duration of the HF oscillations, however, can be established from the electrocardiogram. The pathologically changed atrioventricular conduction may explain the passage of abnormal impulses leading to the supraventricular tachycardia often encountered in patients with WPW syndrome. The TsÊ loop is almost circular because of phase difference in repolarization potentials. This is caused by the left ventricular hypertrophy. (Roentgenologic heart volume is 450 ml./M.^{2} of body surface.)

supports the view that a limited portion of conductive tissue or myocardial fibers, which transmit pathologic impulses of HF character from the atria to the ventricles, is responsible for the changes at the beginning of the QRSsÊ loop. Nor is it impossible that this pathologically changed part of the conduction is responsible also for the occasional spread of rapid impulses, leading to paroxysmal attacks of supraventricular tachycardia. However, no conclusions can be drawn as to the localization of this pathologically changed conductive portion, or as to whether the impulses are transmitted by single or multiple pathways.

As concerns the VCG in Fig. 2, there are widespread HF details in the QRSsÊ loop, causing retardation of the QRS complex with electrocardiographic pattern

of LBBB, although there are vectorcardiographic signs which point to defective intraventricular conduction only. It must be emphasized that not all cases of BBB reveal HF pattern. It is probable, indeed, that both kinds of conduction disturbance, the BBB and the intraventricular defective conduction, occur independently of one another. In the BBB the QRSsÊ loop is angular, because of sudden changes of the potential and of the direction of its instantaneous vector, while the defective intraventricular conduction shows undulations of HF character. Consequently, we have here the possibility of differentiating BBB from defective intraventricular conduction in cases showing increased duration of the QRS complex.

Undoubtedly, HF pattern may be considered a pathologic finding. In the normal material, comprising 24 males and 26 females between the ages of 18 and 69 years, there was in some cases a single notching, which probably lacks all pathologic significance. But notchings over a considerable portion of the loop are always a sign of changed myocardial conduction of the depolarization wave. Because HF details can be encountered at any age and in any heart muscle disease, it is hardly justifiable to relate them to any special etiological factor. Yet there is reason to assume that the phenomenon is common in inflammatory processes of the myocardium, especially in conjunction with a notable enlargement of the heart. This concerns myocardial infarction, too. Anyhow, one gains the impression that large and diffuse myocardial changes are responsible for the conduction change that gives rise to HF details in the VCG. In the case of myocardial infarction referred to in Case 1, there were HF details in connection with a marked enlargement of the heart. Similarly, in a thallium-poisoned dog with diffuse myocardial damage the HF pattern did not become manifest until the very final stage when the heart was enlarged and the VCG showed a total discordance between the QRS and T vectors. In the earlier stages of the condition a successively increasing phase difference in the TsÊ loop could be observed. The HF pattern appeared when there was no longer any phase difference in the TsÊ loop, and when its discordance with the QRSsÊ vector had reached a maximum. Necropsy revealed diffuse and severe myocardial damages in a markedly enlarged heart.[2] There is also evidence—and the case of rheumatic myopericarditis reported in this paper supports this view—that the HF vibrations are reversible when the heart volume decreases. In the case referred to above it decreased from 735 to 410 ml./M.[2] when the QRSsÊ loop was smooth.

If HF details are present, we must obviously expect the conductivity to be influenced by different pathohistologic factors, such as edema, myofibrotic tissue, cell infiltrations, and, probably, hypertrophied myocardial fibers.

CONCLUSIONS AND SUMMARY

1. The cathode-ray tube permits vectorcardiographic recording of HF details of the QRSsÊ loop with great accuracy, provided the frequency range curve of the amplifiers is essentially flat up to 1,000 c.p.s. or more. The high, sweeping velocity of the cathode-ray, which is necessary for the electrocardio-

graphic recording of these details, has a practical disadvantage. Moreover, in electrocardiography, potential variations are registered as linear deflections only.

2. The recording instrument of the ordinary electrocardiograph does not respond to HF details, such as repeated small undulations in the pathway of the QRS-vector head, mainly because the mass of the recording instrument is a physical hindrance.

3. The unresponsiveness of the electrocardiographic recording to HF details leads to time delay during the QRS complex, causing the latter to increase in breadth. In a case of WPW syndrome, HF details in a strictly limited part of the QRSsÊ loop were responsible for the typical delta wave seen in pre-excitation. Similarly, the vectorcardiographic diagnosis of the HF pattern affords a possibility of differentiating defective intraventricular conduction from bundle branch block in case of time delay during the QRS complex.

4. A single notching, which now and then can be seen in normal cases, probably lacks all pathologic significance, whereas repeated HF details of constantly repetitive pattern occur in different myocardial conditions. Of all etiological causes reviewed in this study there seemed to be a certain preponderance of HF changes in heart enlargement due to myocarditis and myocardial infarction. Age, and increase of heart volume for other reasons, did not seem to have any effect on this detail.

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Cardiac Rehabilitation: A Survey of Cardiologists' Opinions

Bryan Williams, M.D., Dallas, Tex., Paul D. White, M.D., Boston, Mass., Philip R. Lee, M.D., Palo Alto, Calif., and Howard A. Rusk, M.D., New York, N.Y.

INTRODUCTION

Increasing interest in "cardiac rehabilitation," not only by physicians, but by public, governmental, and voluntary agencies, has demanded that the medical profession give a satisfactory definition of this term. Direction is also needed for the future energies to be expended in cardiac rehabilitation by those interested in this problem.

As part of a national survey of cardiac rehabilitation, sponsored by the National Heart Institute, a questionnaire was sent recently to a number of the nation's leading cardiologists and internists who have had broad experience in cardiology, asking their definition of the term, their opinions as to how rehabilitation of the patient with cardiac disease is most effectively accomplished, as well as what future course should be taken in assuring the cardiac patient of his place as an effective member of society. The opinions of 36 of these physicians are contained in this paper. It should be emphasized that these are doctors with consulting practices, who daily face the problems of the patient with a diseased heart. The questions posed and a summary of the answers follow:

1. Q. What would you consider a proper definition of rehabilitation, especially as applied to persons with cardiovascular disease?

A. Two examples of excellent definitions reflecting the opinions of most of the group were given by Dr. Roy W. Scott, of Cleveland, and Dr. Clarence E. de la Chapelle, of New York. Dr. Scott: "A rehabilitated cardiac patient is one who, within the physical limitation of his disease, has been psychologically oriented to accept his limitations, and who has been returned to a productive and gainful status in his community within these limitations, without fear or anxiety, and with a sense of usefulness in his own eyes and in those of his associates." Dr. de la Chapelle: "Rehabilitation, as applied to patients with cardiovascular disease, to me means the art and science of restoring a person to that level of physical and mental activity which is compatible with the functional capacity of his heart."

The theme of the majority of definitions was the restoration of the patients to a useful and happy life, within the limits of their physical capacities. These

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From the Institute of Physical Medicine and Rehabilitation, New York University, Bellevue Medical Center, and the Cardiac Laboratory, Massachusetts General Hospital, Boston, Mass.

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definitions emphasized not only maximum physical restoration, but elimination of fear and anxiety as well. Or, as Dr. William Dock, of Palo Alto, California, expressed it, restoration to an active life with the avoidance of neurotic reaction to organic disease.

2. Q. What do you believe are the major problems faced by the practicing physician in his efforts to rehabilitate individuals with cardiovascular disease?

A. The answers to this question have been tabulated in Table I.

TABLE I. MAJOR PROBLEMS FACED BY THE PRACTICING PHYSICIAN IN HIS EFFORTS TO REHABILITATE INDIVIDUALS WITH CARDIOVASCULAR DISEASE

PROBLEM	NUMBER OF CARDIOLOGISTS LISTING PROBLEMS, ACCORDING TO DEGREE OF IMPORTANCE		
	FIRST	SECOND	THIRD
Elimination of fear on the part of the patient and his family	17	6	
Iatrogenic overrestriction by the patient's family physician	5	5	
Difficulty with compensation laws and attitude of industry toward hiring cardiac patients	3	5	8
Medical problems (actual treatment of patient)	4	1	2
Keeping patients restricted within the limits of their physical capacity	2		
Personal economic problems of the patient	1	3	2
Inaccuracy of previous diagnosis	2		

The problems considered to be most important directly involve the relationship of the patient and his physician. The necessity for the physician to eliminate fear about heart disease was considered to be the major problem. Five physicians found as their major problem in dealing with private patients the elimination of overrestriction and undue fear produced by the overcautious advice of other physicians.

The elimination of fear and insecurity in the patient with heart disease, which is the first step in returning the patient to a useful life, can be accomplished largely by the efforts of the patient's own physician. The problem of the oversolicitous family in creating fear and imposing undue restriction was mentioned as a frequent deterrent to full cardiac rehabilitation.

Unwarranted fear about heart disease by industry is also a deterrent to cardiac rehabilitation. This fear appears to be based on: (1) the interpretation of some state workmen's compensation laws to indicate that any myocardial infarction occurring during working hours is due to work per se, regardless of the circumstances, thus making industry liable; and (2) the concern that the working cardiac patient represents an actual physical threat to both himself and his fellow employees.

This fear appears to be based on potential, rather than actual threats, since

it has been demonstrated that most myocardial infarctions actually occur away from work. It has also been demonstrated repeatedly that most cardiac patients, when properly placed, are efficient workers, fully able to meet the demands of a competitive labor market, and represent no threat to themselves or to their fellow workers.

Only 2 cardiologists found it necessary to urge their patients to undertake significantly less activity following discovery of heart disease.

3. Q. What do you think should be done to solve some of these problems?

A. The answers to this question have been tabulated in Table II.

TABLE II. PROPOSED SOLUTIONS TO THE PROBLEMS FACED BY THE PHYSICIAN IN THE REHABILITATION OF CARDIAC PATIENTS

PROPOSED SOLUTIONS	NUMBER OF CARDIOLOGISTS REPORTING
Education of patient and family by the physician	12
Community education about heart disease—including education of management and labor	11
Better education of physicians	11
Modification of workmen's compensation and insurance laws	9
Increased social insurance to relieve the burden of illness	4
Wider use of work classification units	3
Increased facilities for vocational counseling	1

Dr. Charles C. Wolferth, of Philadelphia, furnishes the consensus of opinion in stating that the "problems are those of education." Dr. Irving Wright, of New York, emphasized the challenge that the physician himself should be the key to solving these problems of education. As would be expected from a group of practicing physicians, the emphasis was on the relation of the patient and his physician. In only 3 instances was the wider use of work classification units mentioned. A fourth of the replies acknowledged the help that would be obtained from modification of existing workmen's compensation and insurance laws. This is, however, a problem that, in our opinion, based on an extensive survey, demands more attention than that suggested by the percentage of emphasis given it by the answers to Question 3.

4. Q. In the order of their importance, what measures have you found of value in the rehabilitation of your cardiac patients?

A. Almost universally, a careful, sympathetic, and, particularly, an unhurried discussion with the patient regarding the nature of his heart disease was considered the first and most valuable procedure in cardiac rehabilitation. It was emphasized that this should begin early in the course of the illness and should be continued during all subsequent interviews.

Most consultants felt that of equal importance after recovery is a trial of the patient at his usual occupation with as few modifications as possible.

Consultation with persons trained in related fields, such as social service, vocational counseling, etc., was thought to be occasionally helpful. Several doctors expressed disappointment with their experiences in such consultation.

Dr. Irving Wright asserted that the primary responsibility for the rehabilitation of the patient should be held by the physician and should not be "turned over" to those in related fields; and in this we concur. The chief value of these services was thought to be in dealing with the indigent population; many of the consultants thought these services had little help to offer the doctor in dealing with private patients. However, occasional help with very specific problems by ancillary agencies was thought to be of great value.

5. Q. Please comment on your practical experience in the rehabilitation of patients with the following cardiovascular diseases: (a) congenital heart disease, (b) rheumatic heart disease, (c) hypertensive cardiovascular disease, (d) coronary artery disease, (e) cerebral vascular disease, (f) neurocirculatory asthenia, (g) iatrogenic heart disease, (h) syphilitic heart disease, (i) subacute bacterial endocarditis.

A. *Congenital heart disease:* The group with congenital heart disease was felt to hold the most promise of cardiac rehabilitation, because so many lesions are correctable or, at least, improvable by surgery. Even when only improved by surgery, patients were greatly helped psychologically, feeling that something had "really been done" for them. Opinion was expressed that the publicity attendant upon the more dramatic operations had been of great help in public education about heart disease.

Rheumatic heart disease: Rehabilitation of patients with rheumatic heart disease was thought to be largely dependent on the severity of the active rheumatic fever, degree of valvular deformity, and presence or absence of accompanying congestive failure. Great help has come from surgical correction of mitral stenosis.

Hypertensive cardiovascular disease: It was felt that most patients with hypertensive cardiovascular disease could carry on active, useful lives, particularly with the aid of modern drug therapy in the more severe forms of the disease.

Coronary artery disease: The experiences with patients in this classification were largely covered in answers to other questions. Two major difficulties mentioned were the problems in returning patients to work when the compensation laws were unfavorable, and the slowness in returning patients to work when they were fully covered by sickness insurance. It was emphasized that the majority of patients do recover from myocardial infarction to a sufficient degree to return to their previous work with little or no modification in their activities.

Cerebral vascular disease: In the group of patients suffering from cerebral vascular disease one finds the best results from the help afforded by special rehabilitation centers and techniques. There was much enthusiasm for the great advances in treating patients who have had "strokes."

Neurocirculatory asthenia: Patients with neurocirculatory asthenia were thought to be the most difficult group of all to handle. It was noted that these patients require constant effort on the part of the physician, and that they frequently have very deep-seated emotional problems. Results of psychiatric therapy have been quite variable.

Iatrogenic heart disease: Patients in this category form an important group because of the disease's frequency. Moreover, as was pointed out by one consultant, it may be as completely and dramatically cured by the physician's efforts as are some forms of congenital heart disease by surgery.

Syphilitic heart disease: Syphilitic heart disease was considered to be a "dying disease."

Subacute bacterial endocarditis: Rehabilitation of patients in this group was usually thought to be dependent on the degree of pre-existing valvular damage, as well as on the damage caused by the offending organism. It was pointed out that the outlook for restoration to an active life is now quite good in most patients with this disease, whereas formerly the mortality was almost 100 per cent.

6. Q. Give five or six examples of rehabilitation from your own practice.

A. Many aspects of cardiac rehabilitation were emphasized in the answers to this question. There were examples of a long and useful life after myocardial infarction, and dramatic restoration to full activity following cardiac surgery. One prominent cardiologist cited the example of his own parents. His father lived a full life for 48 additional years after a diagnosis of angina pectoris had been made at the age of 36. His mother played golf several times a week until she was in her seventies, despite long-standing rheumatic heart disease. This physician felt, quite rightly, that there was a great element of "self-rehabilitation" in these two remarkable people.

CONCLUSIONS

A review of the answers to our questions indicates that there is a fairly clear idea, in the minds of physicians at least, as to the meaning of cardiovascular rehabilitation. It is also evident that these practicing physicians believe that the most important factors in cardiovascular rehabilitation are: (1) the proper medical treatment of the patient, so far as disease processes are concerned; (2) the proper attitude of doctor and patient about the disease itself, with emphasis on the possibility or probability of a return to a useful life and the elimination of fear concerning heart disease; (3) the need of correcting certain difficult customs and laws with respect to disability, compensation, and decision of unemployability by various industries; and (4) in apparently rather rare cases, the utilization of work classification units and their facilities for vocational counseling.

Rehabilitation has been proved possible in the majority of cardiovascular conditions, including congenital heart disease, rheumatic heart disease, hypertensive cardiovascular disease, coronary heart disease, and subacute bacterial endocarditis. There are two conditions in which it is still relatively difficult, namely, cerebral vascular disease and neurocirculatory asthenia. However, emphasis should be put on the favorable longevity of individuals with neurocirculatory asthenia and the fact that they often "outgrow" some of their difficulty as they adjust themselves to their problems. All the physicians queried have had interesting experiences in the rehabilitation of their cardiac patients, the rehabilitation coming sometimes through the physician, but at other times through the ability of the patient himself to adjust to his difficulties.

Dietary Fat, Serum Cholesterol Levels, and Incidence of Atherosclerosis and Hypertension in Delhi, India

S. Padmavati, M.R.C.P. (Edin.), M.R.C.P. (Lond.), S. Gupta, M.B.B.S., and G. V. A. Pantulu, M.Sc., New Delhi, India

Four hundred and eighty-six male industrial mill workers and 566 persons (222 males and 344 females) from a rural population group were studied.[1] Their ages ranged from 10 to 70 years. The incidence of atherosclerosis as judged by history of angina or myocardial infarction and/or positive ECG was nil in the industrial workers, and 1.3 per cent in the rural group. The incidence of hypertension was 1.2 per cent among the industrial workers, and 2.6 per cent in the rural population. Complete dietary histories were obtained by the individual questionnaire method, and the average fat intake per day among the industrial workers, rural men, and rural women was 68, 67, and 38.5 Gm., respectively, accounting for 24.5, 24.1, and 17.3 per cent of the total calories, respectively. Serum cholesterol levels estimated by the method of Zak and associates[2] (1954) in 466 cases showed average levels of 168, 183, and 176 mg., respectively, in the 3 groups mentioned. There was a slight but not significant rise of serum cholesterol levels with age in the three groups. There was, however, no correlation between the serum cholesterol level and the daily fat and cholesterol intake. This data, from the first large-scale study in India of this kind, was compared with data from other countries. The figures were very different from those obtained in North West Europe and the U.S.A., and resembled data from Italy (Naples and Bologna), Cape Coloreds, and the Bantus in South Africa.

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From Lady Hardinge Medical College, New Delhi, India.
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The Treatment of Angina Pectoris and Other Muscular Pain Due to Ischemia With Iproniazid* and Isoniazid*

Pedro Cossio, M.D., Buenos Aires, Argentina

Both Cesarman[1] and Cossio[2] have shown independently that iproniazid phosphate is active in the prevention of pain in angina pectoris and intermittent claudication, although to a quite different degree despite the similarity of the doses used. Cesarman obtained a total response in all 41 patients subjected to treatment with this drug. Cossio, experimenting with 36 patients, obtained complete disappearance of pain in only 40 per cent of the cases studied, and a considerable attenuation of pain in 30 per cent, i.e., was successful in 70 per cent and failed in 30 per cent of the cases treated. Furthermore, Cossio has obtained similar effects with isoniazid (although to a lesser extent in angina pectoris) and found iproniazid very effective against the excruciating pains of impending gangrene. At present, a wider experience after a longer observation period has enabled the author to present a more accurate appraisal of results, together with a better knowledge of the indications, contraindications, and convenient dosage of these drugs.

MATERIALS AND METHODS

The subjects for the experimental studies were 120 patients suffering from angina pectoris, diagnosed clinically on the basis of the classical subjective symptoms of this condition and confirmed by electrocardiographic changes, at rest and after standardized effort, suggestive of coronary failure. These patients were classified in 3 grades according to the severity of their complaint as evinced by its progressive nature and by the characteristics of their attacks of pain: Grade I: 65 patients suffering from chronic angina pectoris on selective exertion or violent emotions only, controllable by means of nitroglycerin; Grade II: 45 patients suffering from chronic angina pectoris at the slightest exertion or excitement, still controllable by means of nitroglycerin, although less rapidly so on occasion; and Grade III: 10 patients suffering from subintrant angina pectoris, with pain arising spontaneously at any time in the day, the attacks being more prolonged, more severe, and less effectively controlled with nitroglycerin, and sometimes requiring morphine.

From the Cossio Foundation, Las Heras 2393, Buenos Aires, Argentina.
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Of the patients studied, 88 were male and 32 female. The age range was 35 to 78 years. Their coronary complaint was from 17 years to 2 weeks old. Thirty-seven of the patients had suffered from acute myocardial infarction at least once before. Accompanying conditions included hypertension (59 cases), diabetes (17 cases), and rheumatic cardiopathy (10 cases of aortic stenosis and/or insufficiency, and 2 cases of mitral stenosis).

All the patients had been receiving standard treatment: restriction of effort or complete rest, according to the severity of the condition, and long-acting nitrites plus phenobarbital if no arterial hypotension was present. Some patients were on antithyroid drugs; those with impending myocardial infarction were on anticoagulants. One patient was receiving small doses of thyroid to control myxedema due to I^{131}.

The 36 patients studied in the beginning had to record daily, for 2 weeks, all details relevant to their attacks, e.g., frequency, intensity, precipitating factors, nitroglycerin consumption, and morphine requirement, if any. The 84 patients who were studied subsequently were asked to recall these data from the recent past.

Standard treatment was then suspended (except for anticoagulants, if any were being used), and without altering the patients' daily activities, iproniazid was administered to 85 of them, in doses of 50 mg. every 8 hours for 3 consecutive weeks, and isoniazid to the other 35 in doses of 100 mg. every 8 hours for 3 weeks. The last 100 patients to be studied were told to decrease their doses, first by one third, then by one half, should their attacks of pain subside considerably or disappear altogether, particularly if weakness, faintness, syncope, impotence, or paresthesia should occur. Every patient had to keep a daily record of all details relevant to his attacks.

After a 3-week course, all patients were evaluated by another clinical, roentgenologic, and electrocardiographic examination, including an effort test if electrocardiographic changes had been absent previously. The following courses of action were adopted: (1) The drug was withdrawn from 10 patients whose attacks of pain had ceased altogether; they were told to resume treatment should pain recur. (2) The drug was replaced for 2 to 4 weeks by outwardly identical placebo tablets in 10 patients whose attacks had also ceased altogether. (3) Iproniazid was replaced by isoniazid in 10 patients who had improved considerably with iproniazid. (4) Isoniazid was replaced by iproniazid in 18 patients who had not improved with isoniazid. (5) The remaining patients—provided they had improved to some extent—continued to receive the drugs either intermittently or uninterruptedly for up to 6 months; 7 patients declined to continue treatment because of side effects.

Iproniazid and/or isoniazid was administered also in similar doses for a maximum observation period of 4 months to 10 patients suffering from intermittent claudication of the lower extremities and to 2 patients with impending gangrene of the lower extremities. The appraisal of results was based in the first group on the distances they could cover without pain, and in the second group on the remission or disappearance of spontaneous, chiefly nocturnal, pain.

RESULTS

The results may be divided into three different, yet closely related, categories: (1) the effect of iproniazid and isoniazid on pain, (2) the influence of these drugs on the natural course of the disease, and (3) the side effects of the drugs.

Effect on Pain.—In one third of the patients with angina pectoris who were treated with iproniazid, and in one sixth of the patients treated with isoniazid, the attacks of pain subsided entirely or almost entirely after 3 to 7 days (usual response); in some instances improvement was noted at the first day (early response) or after the second or third week (late response). Again, one third of the patients treated with iproniazid and one sixth of those treated with isoniazid experienced a reduction in the frequency of the attacks down to half the previous number, or to less than half; this involved particularly nocturnal pain and pain due to emotion. The intensity and duration of the attacks diminished, too.

When treatment was interrupted, the symptoms almost invariably returned within 1 to 2 weeks; yet sometimes they returned as late as 4 to 5 weeks afterward. On the other hand, those patients who had shown little or no improvement with 150 mg. of iproniazid or 300 mg. of isoniazid daily were not favorably influenced by an increase to 200 and 400 mg., respectively, except in some instances when pain was partially relieved but never disappeared.

The substitution of isoniazid for iproniazid brought about a recurrence of pain in half the patients; occasionally the recurrence was less frequent and less severe than before. When isoniazid, having proved ineffectual, was replaced by iproniazid, pain subsided, even disappeared, in half the patients.

The effects of both iproniazid and isoniazid on pain lasted for as long as the drugs were administered, except in 5 per cent of the patients in whom pain recurred in spite of the drug, although with less intensity and duration.

Neither iproniazid nor isoniazid prevented the appearance of pain whenever acute myocardial infarction supervened, as will be shown.

The effect on pain due to intermittent claudication was less dramatic. Half the patients reported that they could cover longer distances; yet in the end pain always forced them to stop and rest. No changes were noted by the other patients. The pain of impending gangrene was markedly relieved, but the small number of cases treated allows no conclusions to be drawn with certainty.

Effect on the Course of the Disease.—The present study indicates that neither iproniazid nor isoniazid has any effects whatever on the natural course of angina pectoris: pre-existing electrocardiographic signs persisted or continued to show the usual progressive or regressive changes irrespective of the variations of pain; the effort test remained positive, moreover, although it gave rise to no more pain in many instances. The above statement is further substantiated by the fact that during treatment, and despite the disappearance or attenuation of pain, 1 patient died suddenly and 6 patients were stricken with acute myocardial infarction. In all these instances the corresponding electrocardiographic changes were observed; 5 of the patients required morphine, and 2 died from irreducible collapse. No pain was observed in only one instance, which began as a syncope and was later shown by electrocardiograms to be a typical acute infarction of the diaphragmatic wall of the heart.

The cases of intermittent claudication gave no sign of any favorable variation in their clinical course. The color, temperature, and arterial oscillations remained unchanged in the distal segment of the lower limbs. On the other hand, one of the cases of impending gangrene showed, in addition to the disappearance of pain, an improved blood supply, which ruled out a probable amputation. Nevertheless, this isolated fact will require further confirmation.

Side Effects.—Two thirds of the patients studied reported the following side effects, in the order of their frequency: faintness, weakness, paresthesia, nervousness, syncope, impotence, and muscular twitchings.

As a rule, side effects occurred after the third, fourth, or even the fifth week of treatment with iproniazid or isoniazid (sometimes with iproniazid or isoniazid only; sometimes more strongly with one drug than with the other). With few exceptions, the older the patient was, the greater were the frequency and intensity

of the side effects. The administration of vitamin B_1 or of pyridoxine relieved the side effects only occasionally, but the withdrawal of iproniazid or isoniazid invariably caused them to vanish within 1 to 2 weeks.

The side effects were never serious, but proved to be unpleasant, even incapacitating, in some instances; so much so that the patients would choose to interrupt the treatment in spite of the remission of pain.

Syncope occurred in 5 patients; it was usually transient and took place while the patient was either standing up or sitting or reclining. Syncope while standing happened twice after the use of nitroglycerin, which had been well-tolerated previously. Syncope while sitting or reclining happened to 2 patients with aortic stenosis. It was a prolonged syncope with added convulsions; unfortunately, only one of these patients recovered spontaneously.

Faintness and weakness supervened usually in the erect position: the former especially in the morning after rising or after sharp displacement of the head; the latter set in during the day and also while walking.

MECHANISM

Two different mechanisms have been suggested hitherto in order to explain the effects of iproniazid—and, therefore, those of isoniazid—on cardiac pain and other pain due to ischemia. The "metabolic" mechanism is based on the alleged depressing action of this drug on amine oxidase and other oxidation enzymes, which either saves oxygen or increases its utilization (Cesarman[1]). The "antalgic" mechanism is based on the chemical block of the specific stimulus originating pain, and is supported by the persistence of the electrocardiographic changes and the positive Master sign despite the absence of pain (Cossio[2]).

Recently acquired experience suggests that another mechanism is at work, either metabolic or nervous in nature, which diminishes the excitability and contractility of muscular tissue, with a subsequent decrease in function.

As regards the myocardium, the action of iproniazid entails a moderate diminution in heart rate and frequently, also, a noticeable decrease in blood pressure (which is enhanced at times by the erect posture), as well as the attenuation or disappearance of premature contractions. These effects are responsible for giddiness, weakness, and syncope, particularly after the ingestion of nitroglycerin, which brings about vasodilation.

Side effects are much stronger in elderly people or in patients with a damaged heart, especially if heart failure is present, that is, when the cardiac reserve is impaired. Side effects do not become clinically apparent in young people or in patients with healthy hearts, e.g., tuberculous patients, as shown by the literature.

Moreover, the above-mentioned mechanism explains satisfactorily why iproniazid or isoniazid cannot prevent pain due to great effort or excitement, as is the case with acute myocardial infarction arising during treatment with the said drugs while the patient is more or less free of pain and leading a moderately active existence.

Concerning the skeletal muscles, the mechanism by which the excitability and contractility of muscular tissue are diminished causes an over-all sensation

of weakness, particularly noticeable in the legs upon walking, even to the extent of producing locomotor instability.

INDICATIONS AND DOSAGE

The administration of iproniazid and isoniazid for the prevention of pain is indicated in all cases of angina pectoris regardless of the severity, although these drugs are most likely to be successful when the emotional factor is primary and when the clinical course is least progressive. They may be administered either singly or in combination with anticoagulant therapy, particularly in acute or subacute coronary insufficiency.

Nitroglycerin is not contraindicated. It must be resorted to as freely as before; yet it will be a wise practice for the patient to chew the tablets in a sitting or reclining position in order to prevent syncope, especially if he has already reported faintness. It will also be advisable to instruct the patient as to effort and excitement, both of which should be avoided in spite of the absence of pain, since they might elicit severer and more prolonged pain than usual.

As a rule, the appearance of side effects need not imply suspension of treatment, except in the case of sexual disturbances, which some patients will not forbear, and in the case of recurring giddiness—occasionally the forerunner of syncope—or of syncope itself, fortunately a reversible accident. Although syncope once eventuated in death, this outcome cannot be ascribed to the drug exclusively, since the patient had tight aortic stenosis, a condition in which death is not infrequent.

It will be preferable to begin treatment with iproniazid, whenever this drug is available, since it is more effective than isoniazid, and both of them produce side effects. If the side effects are found to be more severe following administration of one of these drugs, the other should be substituted for it.

Treatment may be envisaged in two different ways. One may start with the larger doses (50 mg. of iproniazid every 8 hours) and, provided no dangerous side effects (recurrent faintness, transient syncope) are noted, one may continue to administer iproniazid until a total, or nearly total, response is achieved, whereupon the doses are decreased to 50 mg. every 12 hours, even to 25 mg. every 8 hours, until the minimal effective dose is found. The opposite course is to start with doses of 25 mg. every 8 hours; these are increased to 50 mg. every 12 hours after one week, and to 50 mg. every 8 hours after another week, until a total, or nearly total, response is achieved—that is, if no serious side effects have occurred to prevent the continued administration of the drug.

The former method has been elected, as a rule; the latter is followed for elderly patients or for those with a damaged heart, and also for relatively young patients with tight aortic stenosis.

If side effects preclude the administration of the larger doses for 3 to 4 weeks, iproniazid should be replaced by isoniazid at twice the amounts being used, inasmuch as the latter drug is at times better tolerated and as effective as iproniazid.

Once pain has subsided entirely, or almost entirely, and the minimal effective dose has been established, treatment must continue indefinitely on a daily basis,

or every other day, or else for 10-day periods separated by 5-day intervals, according to the requirements and the demands of different patients (orgasm and impotence must be taken primarily into consideration).

The drug should not be considered to have failed before 4 weeks of steady administration and 2 more weeks of treatment with doses of 50 mg. every 6 hours have elapsed, provided no serious side effects are observed.

A patient who had formerly received I^{131} against unbearable anginal pains had to be given thyroid subsequently in order to relieve myxedema, whereupon pain recurred but was relieved with iproniazid, which allowed treatment with thyroid to be carried out.

The unpleasant or dangerous side effects of iproniazid and isoniazid can be suppressed only through reduction of dosage or withdrawal of the drug, although at times these effects seem to abate upon administration of vitamins B_1 and B_6.

SUMMARY

The treatment with iproniazid or isoniazid of 120 patients suffering from angina pectoris, and 12 other patients having intermittent claudication and impending gangrene of the lower extremities, has confirmed the results of the author's previous experiences with both these drugs—especially with iproniazid—which have proved highly effective in the prevention of pain due to ischemia. The effects of both drugs on pain itself, on the natural course of the above-mentioned conditions, and the side effects are described. A new explanation as to the mechanism of these drugs is suggested, and the dosage, ways of administration, indications and contraindications are established.

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Lipothymoma Simulating Cardiomegaly: Case Report

Irwin Roseff, M.D., Burton Levine, M.D.,** and Lawrence Gilbert, M.D.****
Newark, N. J.

Large benign lipothymomas are of rare occurrence.[1,2,3] Although they are most often asymptomatic, they may compress adjacent mediastinal structures, resulting in cough, hoarseness, cyanosis, neck vein distention, and edema of the face and upper extremities.[3] Those thymic tumors associated with myasthenia gravis will not be considered in this discussion.

Lipothymomata may closely simulate pericardial effusion, pericardial tumors and cysts, cardiac enlargement,[2,3] and aneurysm of the ascending aorta.[3]

The case to be reported is of particular interest not only because of the rarity of the tumor, but because for 10 years the patient was thought to have had cardiac disease of unknown origin.

CASE REPORT

G. L., a 28-year-old white man, was admitted to the Newark Beth Israel Hospital on March 14, 1957, with the history of having been discharged from military service in 1947, because of an "enlarged heart" discovered on a chest roentgenogram. Attention was brought to the cardiac area because of a murmur at that time. This murmur never was confirmed on repeated examinations. The patient was asymptomatic until 2 years prior to admission when he first became aware of exertional dyspnea, described as deep sighing, and infrequent episodes of "crushing chest pain" lasting 20 to 30 minutes. Yearly chest roentgenograms showed little change in the cardiac enlargement first noted in 1947, until 6 months before admission to the hospital. At that time further enlargement of the heart to the right was noted (Fig. 1,*A* and *B*).

On examination the patient appeared anxious but not acutely or chronically ill. The blood pressure was 120 mm. Hg systolic and 76 mm. Hg diastolic. The cardiac rate was 80 beats per minute; the rhythm was regular. No evidence of cardiac enlargement could be detected on physical examination.

Laboratory data were as follows: Red blood cell count, 5.28 million per cubic millimeter; hemoglobin, 110 per cent (Sahli); white blood cell count, 14,800 per cubic millimeter. The differential cell count was normal. The urinalysis was negative. The fasting blood sugar was 100 mg. per 100 c.c.; blood cholesterol, 160 mg. per 100 c.c.; blood urea nitrogen, 12 mg. per 100 c.c. The serologic test for syphilis was negative. A 24-hour I^{131} conversion ratio was 6 per cent (normal up to 50 per cent). These studies indicated a euthyroid state.

From the Medical Service and Cardiodynamic Laboratory, Newark Beth Israel Hospital, Newark, N.J.
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*Assistant Resident in Medicine, Newark Beth Israel Hospital.
**Associate Attending in Medicine, Newark Beth Israel Hospital.
***Associate Attending in Thoracic Surgery, Newark Beth Israel Hospital.

The electrocardiogram was normal. The chest roentgenogram (Fig. 1,*B*) showed an enlarged triangular cardiac silhouette with the right heart border extending well into the right hemithorax. The left heart border extended 11 cm. to the left of the midline. The interpretation of the Radiology Department was pericardial effusion or pericardial cyst.

Angiocardiography, by introducing 50 c.c. of concentrated Diodrast rapidly into the right antecubital vein and taking exposures at 1.5-second intervals, suggested a space-occupying mass to the right side of the heart (Fig. 2). A pericardial cyst was considered the most likely diagnosis. The patient was discharged, to return at a later date for surgery.

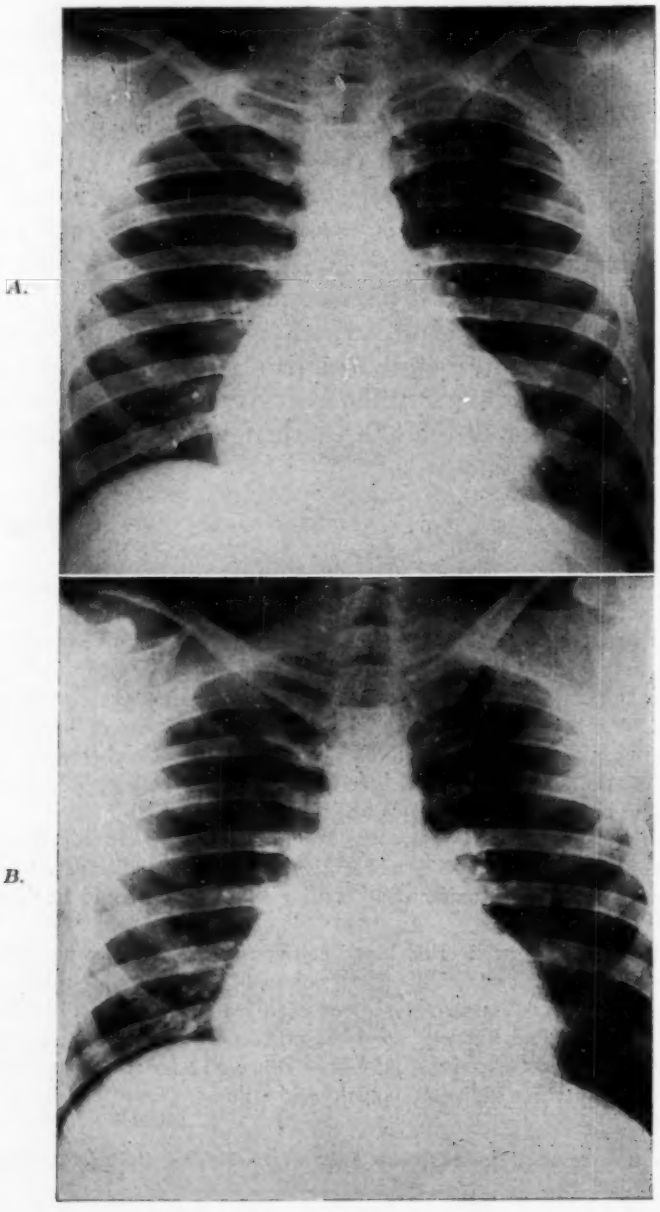


Fig. 1.—*A*, Teleoroentgenogram taken in 1953. Note cardiac enlargement, especially to the right. *B*, Teleoroentgenogram taken in March, 1957. Note further enlargement of cardiac shadow to the right.

He was readmitted to the Newark Beth Israel Hospital on April 14, 1957. The chest roentgenogram and electrocardiogram were unchanged.

On April 16, 1957, the mediastinum was explored through a right posterolateral incision. A large, smooth mass was found overlying the right lateral border of the pericardium, covered by mediastinal pleura. The tumor was "tear drop" in shape, pedunculated, with the apex extending into the superior mediastinum and the convex base just touching the diaphragm. Mobilization of the tumor was simple and the pedicle was dissected free, divided between clamps, and secured with a suture ligature. The patient made an uneventful recovery and was discharged on the ninth postoperative day.

Grossly, the tumor was encapsulated and appeared to be lipomatous in nature, measuring 13 by 12 by 5 cm. and being somewhat flabby (Fig. 3,*A* and *B*). The capsule transmitted a distinct yellowish color. Cross section revealed a uniform, pale yellowish-white, soft, adipose tissue, trabeculated by streaks of fibrous tissue extending from the capsule margin.

Histologically, the tumor was found to consist of extensive areas of ordinary adipose tissue within which were strands of completely mature hyperplastic thymic tissue. This contained masses of typical thymocytes and numerous Hassall's corpuscles, many of which were large, cystic, and degenerated. In addition there were cords of small cells, although larger than the thymocytes, and distinctly epithelial in character (Figs. 4*A*, 4*B*, and 4*C*).

The postoperative chest roentgenogram showed a cardiac shadow normal both in size and configuration (Fig. 5).

Seven months following surgery the patient is well and completely cured of his episodes of chest pain and dyspnea.

DISCUSSION

The rarity of this tumor is evident from the paucity of reports in the medical literature. At the present time we are aware of only 11 cases of lipothymoma

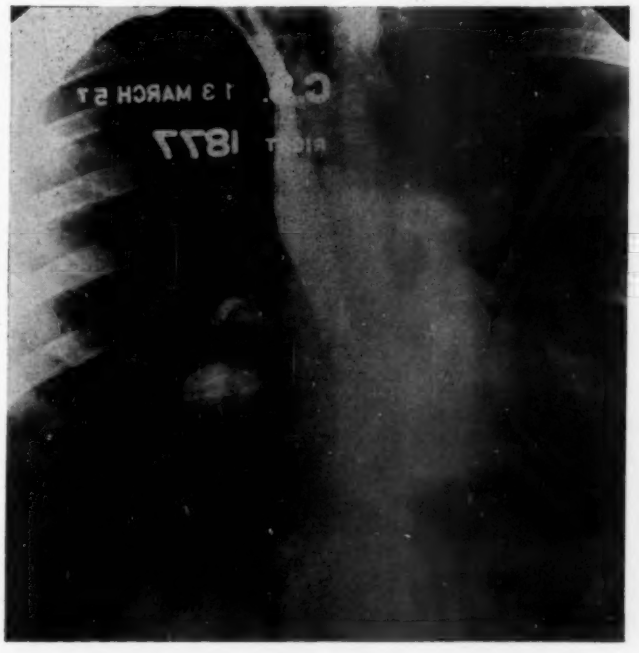
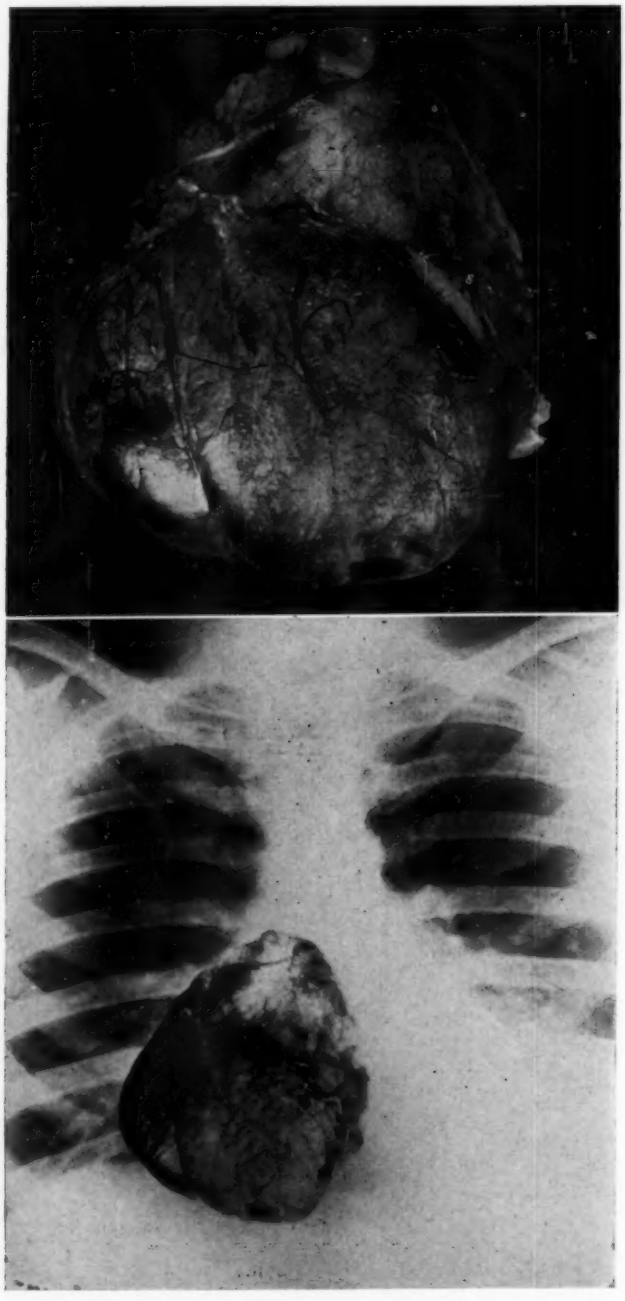


Fig. 2.—Angiocardiogram with dye in superior vena cava, right atrium, and right ventricle. Mass extrinsic to and adjacent to right heart border is visualized.

previously reported in the English literature.[1-3,5-12] Of this group, 4 presented initially as cardiomegaly.[1,2,5,6] It must be stated, however, that since the term thymolipoma was first used by Hall,[6] in 1949, other similar cases may have been reported under the all-inclusive term of thymoma or thymic tumor. Neverthe-



A.

B.

Fig. 3.—*A*, Pear-shaped tumor mass measuring 13 x 12 x 5 cm. *B*, Tumor superimposed on teleoroentgenogram, indicating position in thorax.

less, in the decade since this term has been in use, the infrequency of the tumor is reflected in the few reported cases. Bernstein and associates[1] reported from this hospital the case of a 20-year-old Negro with an asymptomatic lipothymoma which simulated a pericardial effusion. The tumor, weighing 2,810 grams, contained large amounts of fat which, because of its fluidity at body temperature, closely mimicked pericardial effusion.[1]

Rubin and Mishkin[2] presented the case of a 19-year-old Puerto Rican woman complaining of exertional chest pain, with an enlarged cardiac shadow on a chest roentgenogram. At surgery a large lipothymoma was found with the apex attached to the superior mediastinum. Andrus and Foote[5] removed a 2,235-gram lipothymoma from a 13-year-old boy complaining of cough and dyspnea, and Hall[6] reported a lipothymoma weighing 1,100 grams in an accidentally killed 47-year-old man.

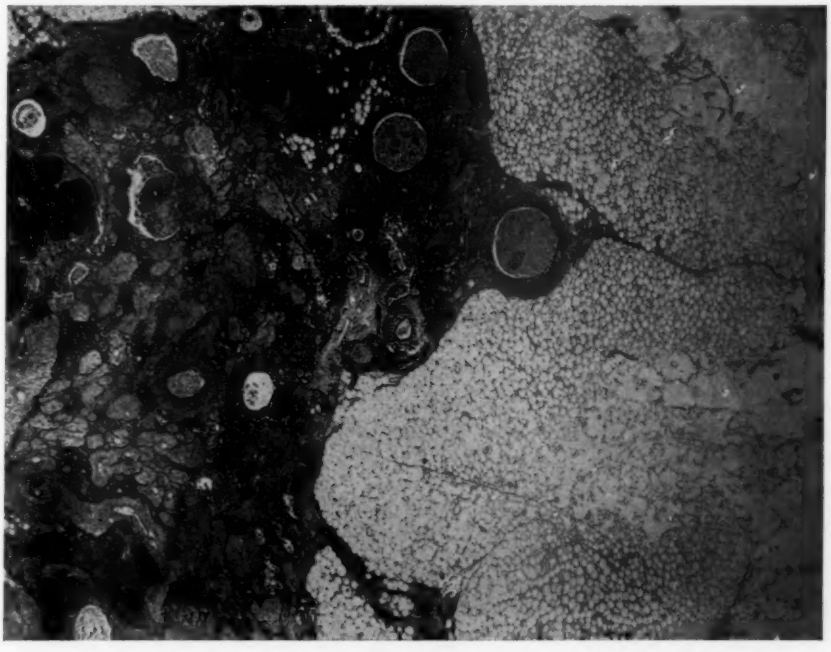


Fig. 4*A*.—Low magnification showing thymic tissue with numerous cystic Hassall's corpuscles, and copious adipose tissue.

Our case was interesting from several points of view. A diagnosis of "cardiac enlargement" was made 10 years prior to definitive diagnostic studies and surgery. The tentative diagnosis was heart disease with cardiomegaly of unknown origin. Yearly chest roentgenograms showed no change in heart size until 6 months prior to hospitalization, at which time further cardiac enlargement was noted. Symptoms of exertional dyspnea were considered iatrogenic, largely because of the description which strongly suggested the hyperventilation syndrome. At this time the pain is still unexplainable.

Angiocardiography was of considerable aid in separating the extracardiac portion of the enlarged cardiac silhouette from the heart itself. The definitive

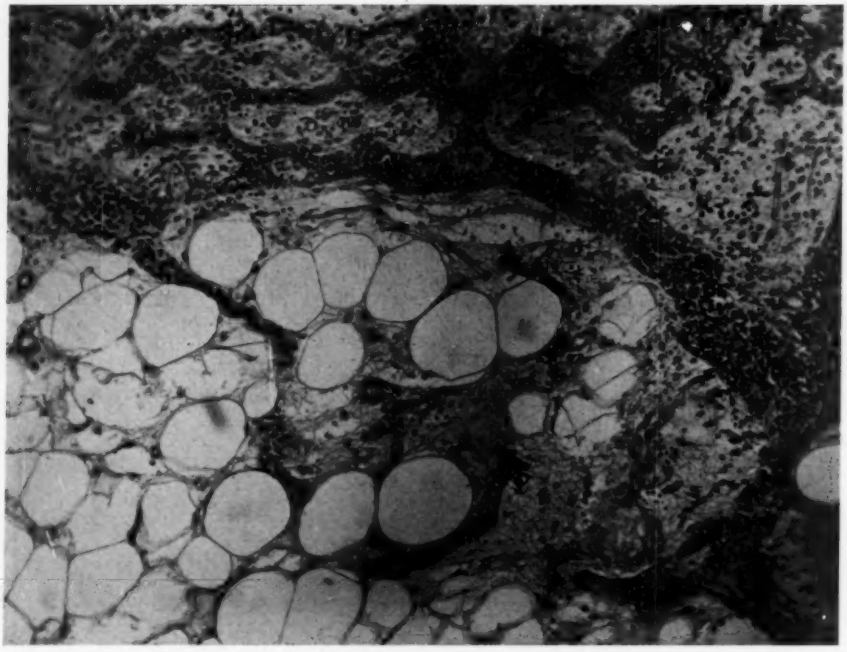


Fig. 4*B*.—Typical thymic tissue showing thymocytes and Hassall's corpuscles.

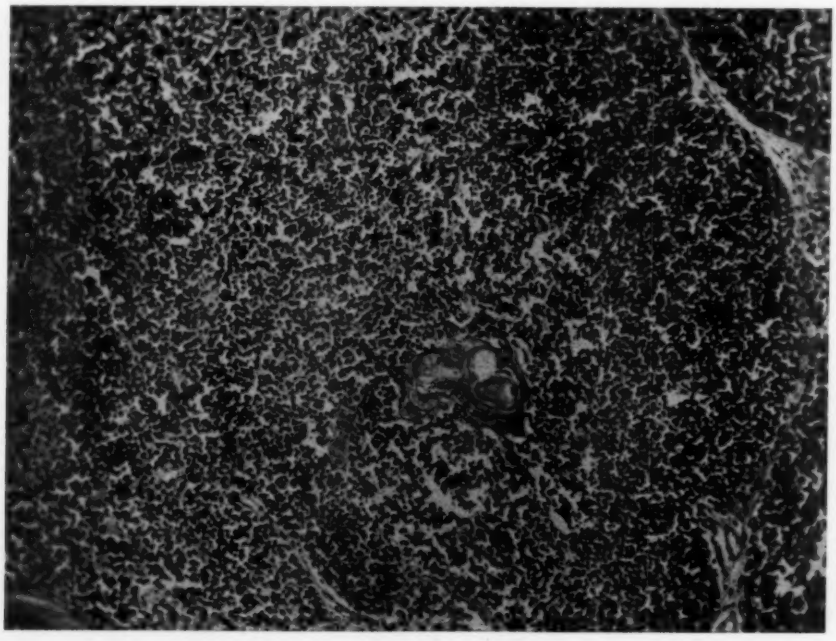


Fig. 4*C*.—Cords of thymic epithelium indicating considerable hyperplasia of this element, and adipose tissue.

diagnosis, however, had to await surgery. Preoperatively the extracardiac mass was thought to be a pericardial cyst or tumor. Here again it should be stressed, as it has been in the past,[1,3] that lipothymoma must be included in the differential diagnosis of pericardial effusion, anterior mediastinal tumors, and cardiomegaly of undetermined origin.

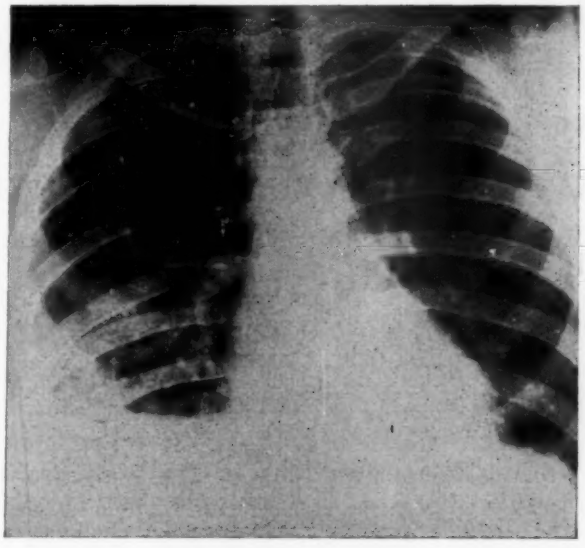


Fig. 5.—Postoperative chest roentgenogram showing cardiac shadow normal in size and configuration.

SUMMARY

1. A case of lipothymoma, presenting as cardiomegaly, in a 28-year-old white man is presented.

2. It is of interest that the patient was declared ineligible for military service because of "cardiac enlargement" 10 years prior to surgery.

3. The importance of including lipothymoma in the differential diagnosis of cardiomegaly is again stressed.

We wish to thank Dr. Simon Frank for permission to study this case, and Dr. Milton Kannerstein for his pathologic analysis.

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Pulseless Disease: Report of a Case

Christ Aravanis, M.D., Stavros Avgoustakis, M.D., and George Michaelides, M.D.
Athens, Greece

Recently we observed a case of pulseless disease, or Takayasu syndrome. Since this syndrome rarely is encountered, clinical reports are still of interest. This is the second case reported from Greece.

CASE REPORT

This case was referred to us by the one of the authors (S.A.) from the island of Rhodes. The diagnosis was that of a peculiar syndrome without pulses in the upper extremities.

Present Illness.—The patient, a 50-year-old man, complains of easy fatigability and weakness in the upper extremities, persisting since 1943. He states that he had been relatively well until about 1953, when he noted the onset of dizziness. For the past 3 years he has had general malaise and weakness of vision. During the same time he has had three episodes of loss of consciousness after sudden rising. For the last 10 months he has noted increase in his dizziness, vertigo, progressive weakness in the upper extremities, particularly after exertion, and numbness in the fingers. These symptoms obliged him to discontinue his work as a truck driver. During this same period he complained of more visual disturbances and fatigue of the muscles of mastication.

Past History.—The patient had the usual childhood diseases. Twenty years ago he suffered from a pain in the left arm, of one month's duration. This pain was characterized as rheumatic in origin, and no mention was made to him about any abnormality. He had had gonorrhea during his stay in Egypt, in 1934, but had been completely treated. The family history was negative. He has smoked about twenty cigarettes daily since the age of 16, but he denies drinking.

Physical Examination.—Physical examination revealed a moderately-developed male, rather asthenic. His pulse was 70 per minute. The blood pressure was unobtainable in both upper extremities. Pulses were not palpable in the radial, brachial, subclavian, innominate, or carotid arteries. The abdominal aorta was easily palpable. In the lower extremities the blood pressure was 180/90 mm. Hg, and the pulses were present and strong. By oscillometry there was no deflection in either of the upper extremities. In the legs deflections were found between 5 and 6. The heart was normal in size. A systolic murmur, Grade 3, was audible in the left supraclavicular fossa, transmitted upward. A Grade 2 systolic murmur was heard at the base of the heart in the left and right second intercostal spaces near the sternum. The rest of the physical examination was negative.

Laboratory Data.—The red blood cell count was 4,600,000. The white blood cell count was 9,500. The differential count was 70 per cent polymorphonuclear leukocytes, 26 per cent lymphocytes, 2 per cent eosinophils, and 2 per cent monocytes. Hemoglobin was 90 per cent, the hema-

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From the Cardiac Clinic of the Heppocration Hospital of the University of Athens, Greece (Prof. G. Michaelides, Director).

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tocrit 44. Blood sugar was 0.97 Gm. Blood urea was 0.44 Gm. Total cholesterol was 281 mg. (Bloor). Prothrombin time was 15 seconds. The erythrocyte sedimentation rate was 45 mm. for the first hour and 76 mm. for the second hour (Westergren). Urine examinations revealed no specific findings. Serologic examinations for syphilis were negative. The ECG was normal. A chest roentgenogram revealed clear lungs, a normal heart, and slightly enlarged aorta. Ophthalmoscopic examination revealed many small venous and arterial aneurysms in both fundi. The pressure of the central ophthalmic artery was unobtainable. No hemorrhages, exudates, or papilledema were found. An aortogram and a muscle biopsy were denied by the patient. He was put on long-term anticoagulant treatment and referred to his family physician, with the diagnosis of thromboangiitis obliterans of the major branches of the aortic arch, and the advice that he be maintained on anticoagulant therapy.

DISCUSSION

A case of the syndrome known as "pulseless disease" is presented. Although the term "pulseless," which was first used by Shimizu, in 1951, is not exact, because only the pulses of the brachiocephalic branches of the aorta are absent, it has been accepted by most authors. Other names given to the syndrome are thromboangiitis obliterans, subclavio-carotica, Takayasu syndrome, and reverse coarctation. About 90 cases have been reported in the world literature up to the present time, and more than 60 of these were published in the Japanese literature. Scattered cases were reported from different countries. The majority of the affected patients were females; very few were males. Usually the syndrome appears in the younger age group, although a few cases in more advanced age groups have been reported. The disease is characterized by progressive narrowing and occlusion of the major branches of the aortic arch. As a consequence the pulse is partially or completely absent in the subclavian and carotid arteries and their branches. The symptoms are due to diminished circulation in the upper extremities and the central nervous system. The patients complain of weakness, numbness, and cramps in the upper extremities, which conditions are precipitated or aggravated by exertion. These symptoms were present in our patient, and obliged him to discontinue his job. Complaints due to inadequate cerebral circulation also are present at some stage of this illness; dizziness, vertigo, fainting spells are the most common. Ocular manifestations were emphasized by the Japanese ophthalmologists, and are considered essential to the diagnosis. All degrees of ocular anemia are present. Peripapillary anastomoses and arteriovenous aneurysms are considered characteristic. Our patient presented all these symptoms and signs. For 11 years his complaints were due to the diminished circulation in the upper extremities. The last 3 years complaints due to the impaired circulation to the central nervous system were added. Today he is unable to perform any work. Moreover, this case is unusual because of two other features: (1) he is a male, and (2) both carotid arteries are involved. The laboratory data show him to have a high sedimentation rate. This finding was present in many of the published cases. A slightly enlarged aorta was also present in our case, but no evidence of aortic aneurysm was revealed by careful roentgenologic investigation.

The pathogenesis of the syndrome is unknown. Histologically the disease is characterized by an inflammatory panarteritis with cell infiltration, and a secondary thrombosis of the arteries. Although the course of the syndrome is

extended over years, the prognosis is poor, and death finally occurs as the result of central nervous system ischemia. No specific treatment exists. Antibiotics, cortisone, ACTH, and anticoagulants have been used without success. Long-term anticoagulant treatment may be beneficial as far as thrombosis is concerned. Endarterectomy or local resection and transplantation of the affected parts of the aorta may be a promising treatment.

SUMMARY

A case of pulseless disease is presented. This is the second case from Greece. The essential findings were complete absence of the pulse in the arms and both carotid arteries. Typical subjective symptoms and objective findings were present because of the diminished circulation in the upper extremities and the central nervous system. Since the number of reported cases is still limited, publications such as ours will focus more attention on this syndrome, with the probability that more cases will be diagnosed.

We wish to thank Dr. A. Hoidakis and Dr. A. Polycratis for their assistance in preparing this paper.

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The Relation of the Aortic Root to the Ventricular Septum in Tetralogy of Fallot

Leonard Leight, M.D., and Lawrence A. Davis, M.D., Louisville, Ky.

The tetralogy of Fallot is described, classically, as consisting of right ventricular hypertrophy, pulmonic stenosis, interventricular septal defect, and dextroposition of the aorta. As a result of the dextroposition of the aorta, the outflow from the right ventricle has been considered to enter both the pulmonary artery and aorta, resulting in a right-to-left shunt.

Recent experience in the surgical repair of this anomaly has cast doubt on the concept of overriding of the aorta in cases which clinically appear to be Fallot's tetralogy. Lillehei[1] has reported complete anatomic correction of the lesion in patients with tetralogy of Fallot, by means of closure of the interventricular septal defect and resection of the infundibular stenosis. Despite the demonstration in the operating room that overriding of the aorta does not occur in at least some cases which fulfill the clinical criteria for the diagnosis of Fallot's tetralogy, there has been little comment in the literature concerning the validity of this observation. Dextroposition of the aorta continues to be described as part of the tetralogy of Fallot.[2,3] However, McCord and associates[4] have recently indicated that overriding of the aorta is probably not an important feature of this anomaly.

During angiocardiographic study of patients with tetralogy of Fallot, it has become obvious that there is not simultaneous filling of the aorta and pulmonary artery from the right ventricle, but rather that there is initial filling of the pulmonary artery from the right ventricle, flow of the opaque material across the interventricular septal defect to the left ventricle, and, only after the latter event occurs, filling of the aorta. The purpose of this report is to provide angiocardiographic evidence in support of this sequence of events.

METHODS

Angiocardiography was performed according to the method described by Kjellberg and associates,[5] utilizing an Elema* biplane angiocardiogram apparatus. This method utilizes the technique of selective injection of opaque material into the central circulation. Films are obtained

From the Departments of Medicine and Radiology, University of Louisville School of Medicine, Louisville General Hospital, and Children's Hospital, Louisville, Ky.

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*Manufactured by Elema, Industrivägen 23, Stockholm, Sweden.

simultaneously in the frontal and lateral positions at rates up to 12 frames per second. All injections were made through special thin-walled catheters with tips modified with 2 extra side lumens, as in the Goodale-Lubin catheter*, in order to minimize recoil of the catheter at the time of injection. Injection was made by means of a hand-pressure injector, using 1.2 c.c. of Urokon† per kilogram of body weight. Cardiac catheterization was performed in the usual fashion.

RESULTS

Results are presented in 3 children who had classical tetralogy of Fallot clinically. All were grossly cyanotic. All had selective angiocardiography performed with injection into the right ventricle. Cardiac catheterization was attempted in 2 of the 3 patients. One patient, W. W., a 1-month-old infant had an angiocardiogram only. In the second patient, M. H., a 4-year-old boy, the pulmonary artery was not entered at the time of cardiac catheterization. The right ventricular pressure in this patient was 92/6 mm. Hg. The third patient, T. M., a 9½-year-old boy, had an infundibular stenosis with a right ventricular pressure of 90/1 mm. Hg. Arterial oxygen saturations were not obtained. In the patient in whom the pulmonary artery was entered, and in the other in whom only the right ventricle was entered, no left-to-right shunt was demonstrated, a usual finding, in our experience, in patients with tetralogy of Fallot.

The angiocardiographic studies performed in these cases are illustrated in Figs. 1 to 3. Fig. 1 (T. M.) illustrates 4 lateral projections, the first film having been exposed 1 second after the start of injection. This case represents a classic angiocardiographic example of the tetralogy of Fallot. The filling of the left ventricle and pulmonary artery from the right ventricle, with no evidence of opacification of the aorta, is well shown in Fig. 1,*A*. In Fig. 1,*B* through *D* subsequent filling of the aorta is illustrated, and in *D* the normal origin of the aorta from the left ventricle is well seen. Fig. 2 (M. H.) similarly illustrates filling of the left ventricle prior to filling of the aorta. Fig. 2,*A* was taken 0.5 second after the start of injection; it shows opaque material in the right ventricle and the beginning of pulmonary artery opacification. Fig. 2,*B* shows opaque material entering the left ventricle from the right ventricle. Opacification of the aorta has not occurred as yet. It is not until Fig. 2,*D* that opacification of the aorta is noted. Again in this case, the aorta appears to be arising entirely from the left ventricle. Fig. 3 (W. W.) is especially interesting in that it demonstrates an example of the tetralogy of Fallot in which there is a hypoplastic pulmonary artery. Despite the presence of a severe pulmonary obstruction, the flow of opaque material is from the right ventricle to the left ventricle and pulmonary artery, with the aorta appearing to arise entirely from the left ventricle. Opacification of the aorta is not seen until Fig. 3,*D*.

DISCUSSION

The correlation between physiologic phenomena and pathologic changes in patients with septal defects, with and without pulmonic stenosis, has recently been presented at length by Edwards[6] and Damman.[7,8] As these authors have

*Manufactured by U. S. Catheter & Instrument Corporation, Glen Falls, N. Y.
†Registered trademark.

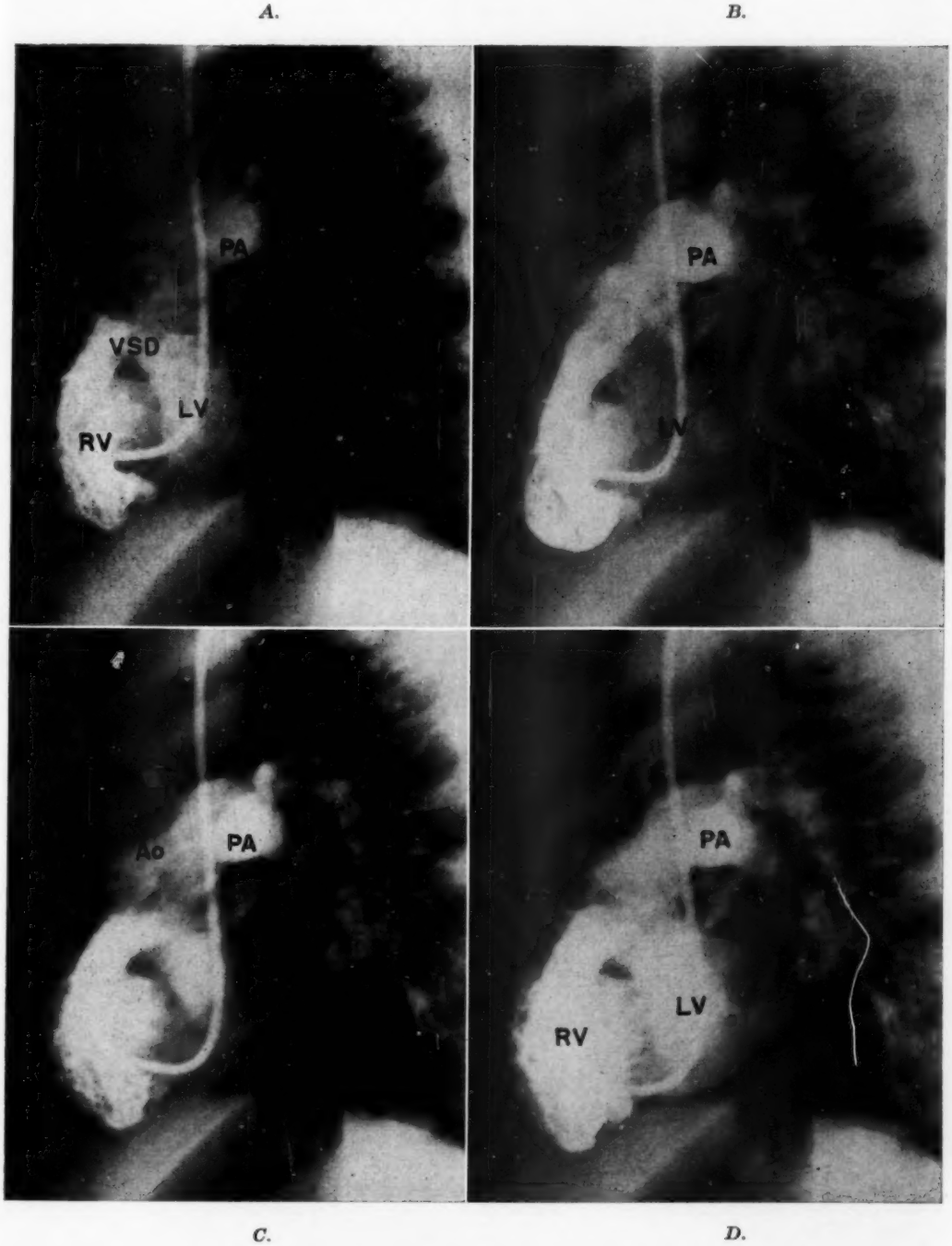

Fig. 1.—Patient T. M. Time of exposure after start of injection: *A*, 1 sec.; *B*, 1⅓ sec.; *C*, 1½ sec.; *D*, $1^5/_6$ sec. Passage of opaque material through the septal defect is well shown in *A*. Opacification of the aorta is not present until *B*.

The abbreviations used in Figs. 1 through 3 are: VSD = ventricular septal defect; RV = right ventricle; LV = left ventricle; PA = pulmonary artery; Ao = aorta.

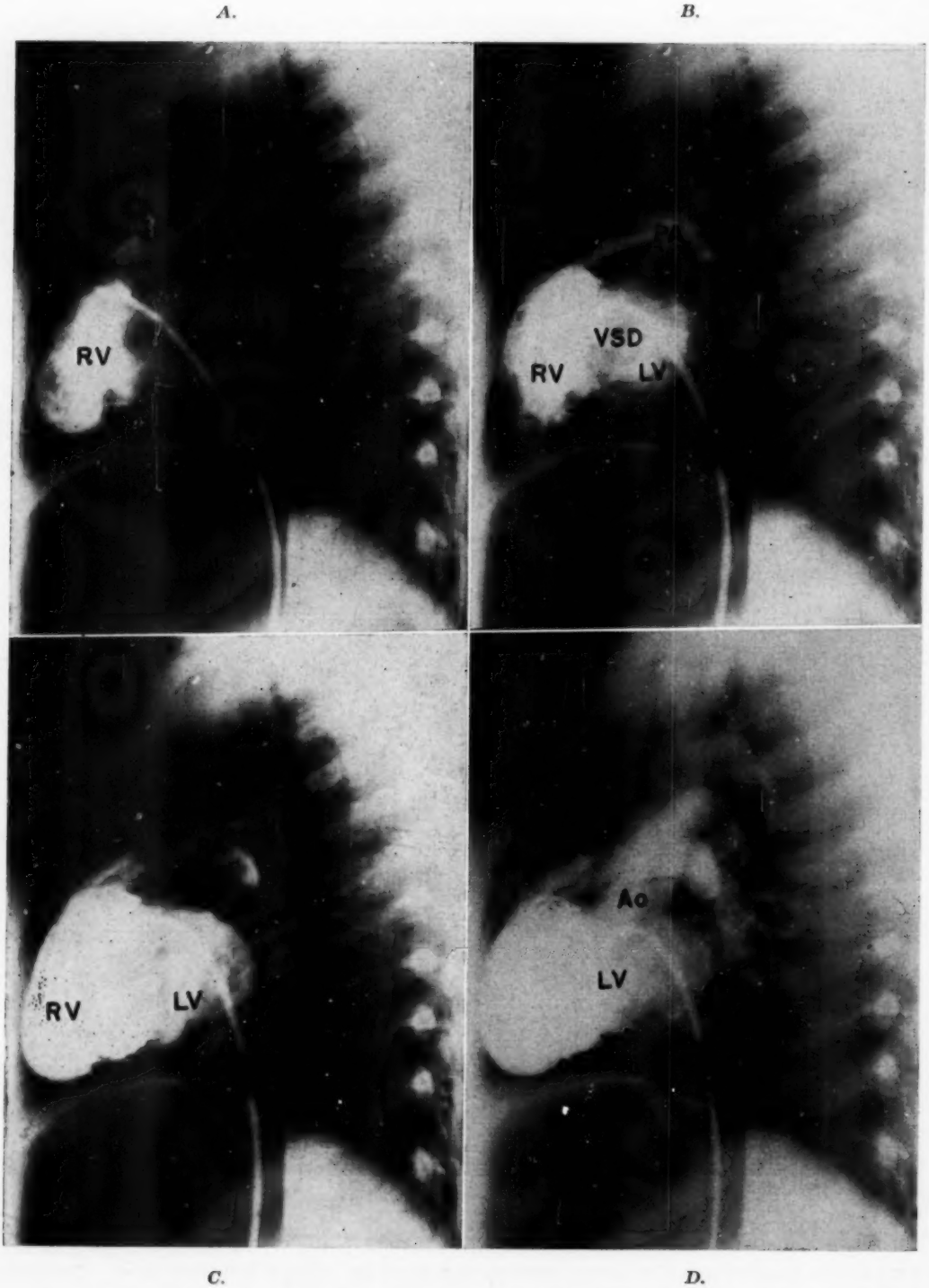

Fig. 2.—Patient M. H. Time of exposure after start of injection: *A*, ½ sec.; *B*, ¾ sec.; *C*, 1 sec.; *D*, 1½ sec. Passage of opaque material through the ventricular septal defect is shown in *B*. Opacification of the aorta is not seen until *D*.

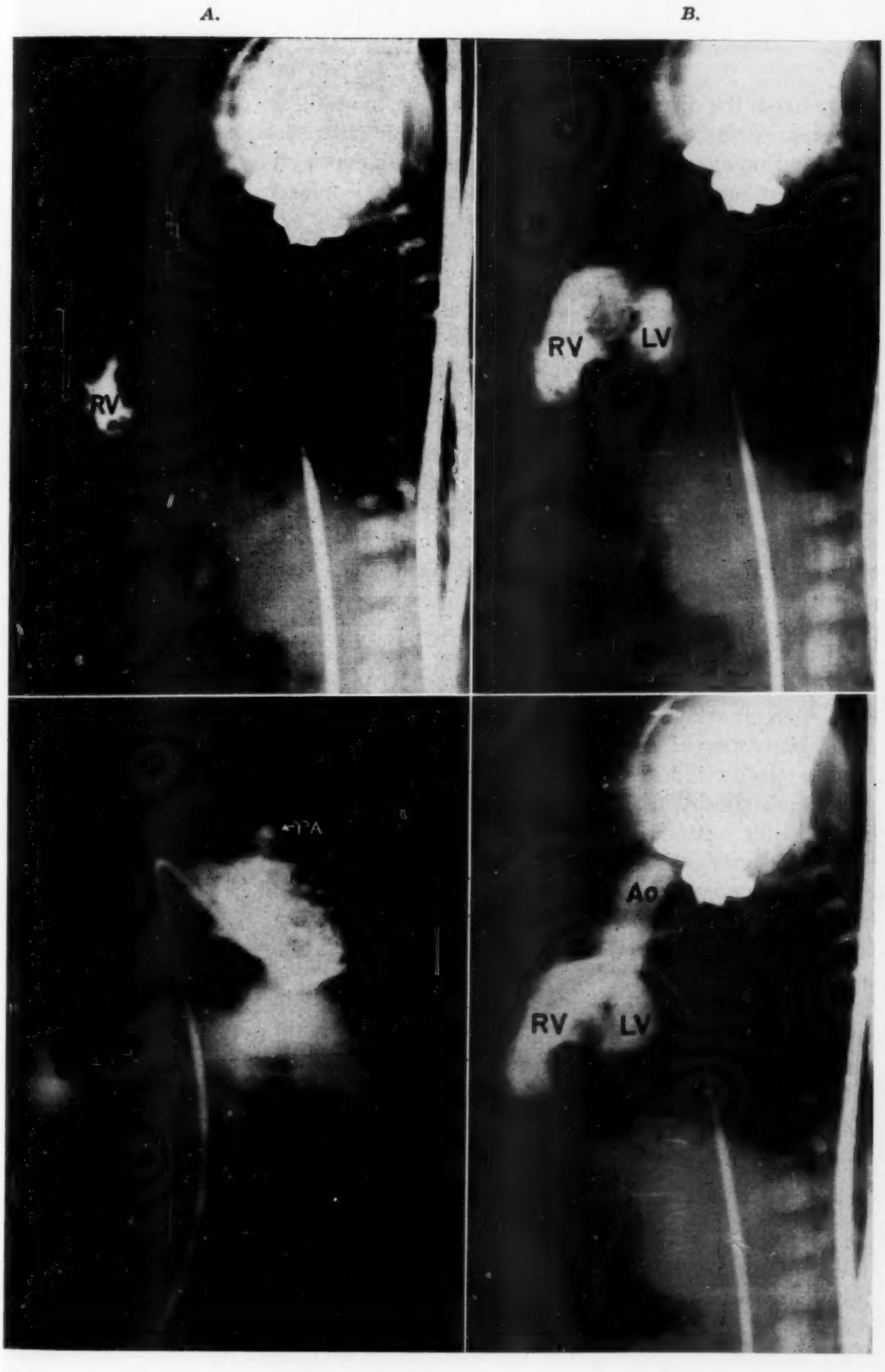

Fig. 3.—Patient W. W. Time of exposure after start of injection: *A*, ⅔ sec.; *B*, 5/6 sec.; *C*, 1⅙ sec.; *D*, 1½ sec. *A*, *B*, and *D* are lateral projections. *C* is a frontal projection, since the pulmonary artery did not reproduce well on the lateral projection. Flow of opaque material through the septal defect is shown in *B*. The aorta is not seen until *D*.

emphasized, the direction of a shunt between the right and left heart in the case of a septal defect is ultimately dependent upon the resistance to flow in the systemic and pulmonic circuits. In this sense, a stenosis at either the outflow tract of the right ventricle or at the pulmonary valve is a locus of resistance analogous to that of an increase in resistance in the pulmonary vascular tree.[6] The occurrence of pulmonic stenosis and interventricular septal defect with a left-to-right shunt and increased pulmonary blood flow has been well documented.[5,9,10] In these cases, one can assume that the pulmonic stenosis is relatively mild.

Noncyanotic cases of tetralogy of Fallot in which pulmonic stenosis was accompanied by a left-to-right interventricular shunt have recently been described by Rowe and associates.[11] These cases, in which filling of the aorta occurred in normal sequence during venous angiocardiography, would appear to be identical from a physiologic standpoint to the cases of interventricular septal defect, pulmonic stenosis, and left-to-right shunt described above. As Rowe and associates[11] emphasize, there is great difficulty in determining whether or not the aorta is anatomically overriding the right ventricle. It is our belief that the fact that the catheter enters the aorta cannot be taken as proof of overriding, since the aorta may be entered via an interventricular septal defect. Since the relationship of the aorta to the ventricular septum is a dynamic one, the determination as to whether or not overriding of the aorta is present is difficult even at autopsy.[12,13] Angiocardiography probably best demonstrates the functional and anatomic relationship of the aorta to the ventricles. Wood and co-workers[14] also have reported cases labeled acyanotic tetralogy of Fallot, which appear physiologically indistinguishable from cases of ventricular septal defect and pulmonic stenosis. It would appear that the designation acyanotic tetralogy of Fallot is not justified and is only confusing in those cases in which overriding of the aorta is not definitely demonstrated.

Our experience indicates that in cyanotic cases which clinically fulfill the classical criteria for the diagnosis of tetralogy of Fallot, the lesion also consists functionally of an interventricular septal defect and pulmonic stenosis, the latter being of severe degree. The three cases presented here are not unique in our experience. In every case of tetralogy of Fallot in which an adequate selective angiocardiogram has been obtained, we have been able to demonstrate that the left ventricle and pulmonary artery fill from the right ventricle prior to opacification of the aorta. Simultaneous filling of the aorta and pulmonary artery did not occur.

There undoubtedly is an anatomic spectrum ranging from slight overriding of the aorta which is physiologically insignificant to cases with marked overriding which has considerable physiologic significance.[5,12-14] When such overriding is complete, transposition of the aorta is present. Even in the presence of considerable anatomic overriding of the aorta, the relationship of the pressures in the two ventricles and in the aorta will determine whether or not the aorta fills from the right ventricle. Whether or not in the cases presented here there is any anatomic anomaly in the origin of the aortic root, we cannot definitely say. However, it is our impression from angiocardiographic studies that normal origin of the aortic root is the usual finding. This appears to be so in the 3 cases shown

here. According to Kirklin,[15] approximately 75 per cent of the patients coming to surgery with tetralogy of Fallot do not have anatomic overriding of the aorta. In approximately 25 per cent of his cases, overriding was anatomically present.

Selective angiocardiography with a speed of at least 6 pictures per second is necessary in order to obtain sufficient detail of the right and left ventricular outflow tracts. When venous angiocardiography is performed, not only is detail lost because of overlapping of structures, but a pulmonic stenosis with a right-to-left interatrial shunt may be mistaken for tetralogy of Fallot. If selective angiocardiography is done with slow exposure speed, passage of opaque material into the left ventricle from the right ventricle prior to opacification of the aorta may be missed. It appears that little is gained by labeling as tetralogy of Fallot those cases of pulmonic stenosis with a right-to-left interventricular shunt. Even clinically such cases may be indistinguishable from cases of pulmonic stenosis with a right-to-left atrial shunt. A more appropriate designation would be one which indicates the site of septal defect, the type of stenosis, and the predominant direction of shunt.

SUMMARY

Three cases of clinically classic tetralogy of Fallot are presented in which angiocardiographic studies demonstrated no overriding of the aorta. These studies indicate that many cases of tetralogy of Fallot should be considered as a type of ventricular septal defect with pulmonic stenosis, in which overriding of the aorta is of no functional or surgical importance.

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Traumatic Laceration of the Anterior Descending Coronary Artery Treated by Ligation Without Myocardial Infarction: Report of a Case With Review of the Literature

Richard A. Carleton, M.D., and Thomas Boyd, M.D.,** Boston, Mass.*

For many centuries trauma to the heart has excited the interest of physicians. Barbette, in 1687, felt that wounds of the heart were invariably fatal, but during the fifteenth and sixteenth centuries several post-mortem descriptions of healed cardiac wounds were found. From Bonetus, in 1700, and Morgagni, in 1730, came the recognition that sudden filling of the pericardium was the major factor causing death, and that all cardiac wounds are not necessarily fatal. The first indication of modern therapy came in 1882, when Black sutured induced heart wounds in rabbits. In 1896, the now famous cardiorrhaphy case of Rehn was reported, as described by Blau.[1]

Since that time, large numbers of cases of penetrating cardiac trauma have been reported. Eleven large series,[2-12] including 783 cases, have a mortality of 42 per cent, a figure which shows little fluctuation over the past 50 years. However, the most recent series are those of individual surgeons, and include cases dying before definitive therapy.

The literature pertaining to traumatic major coronary artery injury is less extensive. The present report concerns a case of traumatic division of the anterior descending coronary artery successfully treated by ligation without subsequent evidence of myocardial infarction.

CASE REPORT

This 22-year-old white man entered the Boston City Hospital, at 10:15 P.M., on May 5, 1957, approximately 5 minutes after being stabbed with a 6-inch penknife while he was intoxicated. The patient complained only of sharp pain in the region of the wound. The family and past histories were noncontributory.

Physical Examination.—Physical examination revealed a regular pulse of 100, a blood pressure of 70/30 mm. Hg, and a respiratory rate of 20. He was a well-developed, well-nourished,

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From the Thorndike Memorial Laboratory, and the Second and Fourth (Harvard) Medical Services, Boston City Hospital, and the Department of Medicine, Harvard Medical School; and the Thoracic Surgery Service, Boston City Hospital, and the Department of Surgery, Boston University School of Medicine.

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*Resident in Medicine, Second and Fourth (Harvard) Medical Services; Assistant in Medicine, Harvard Medical School.

**Resident Surgeon, Thoracic Surgery Service, Boston City Hospital.

cool, pale, sweaty, and intoxicated young man who appeared acutely ill. The pupils were dilated. Head, eyes, ears, nose, and throat were otherwise not remarkable. The neck veins were not distended. On the chest wall there was an incised wound, 1.5 cm. long, in the third intercostal space 3 cm. to the left of the left sternal edge. The lungs were initially clear, but shortly displayed signs of increasing fluid in the left pleural cavity. The apex impulse was not palpable, but the heart was not enlarged to percussion in the supine position. The heart sounds were well transmitted and of good quality with the aortic second sound greater than the pulmonic second sound. There were no murmurs, rubs, or gallops. The peripheral pulses were weak, but there was no paradoxic pulsation. The remainder of the physical examination was noncontributory.

Laboratory Data.—Laboratory studies revealed normal urinalysis, a hematocrit of 42 per cent, and a white blood cell count of 16,800, which gradually fell to normal. The nonprotein nitrogen was 31 mg. per cent, the total protein 6.2 Gm. per cent, and the serum cholesterol 145 mg. per cent. The admission chest x-ray showed left pleural fluid, but was otherwise not remarkable.

Hospital Course.—On arrival at the hospital there had been no audible heart action, but, coincidentally, within seconds after the start of an intravenous infusion of normal saline, heart sounds were well heard, and the blood pressure rose to the range of 70/30-95/68 mm. Hg at the time of the physical examination. Despite transfusion, the blood pressure remained at these levels, and after 2 hours of observation, exploratory thoracotomy was decided upon because of continued shock and progressive left hemothorax. Just prior to incision, after anesthesia and intubation, the neck veins were first noted to be distended, and the blood pressure became unobtainable.

Emergency thoracotomy: At emergency thoracotomy under endotracheal ether anesthesia, approximately 600 to 800 c.c. of dark, partially clotted blood were found in the left pleural cavity. The pericardium was distended with dark, unclotted blood which was oozing from an 1-cm. laceration in its anterior aspect. The pericardium was opened and the left anterior descending coronary artery was seen to be transected at a point 2 cm. below the atrioventricular groove. A brisk pulsatile flow of blood came from the proximal and distal portions of this vessel. Subjacently there was a small laceration of the ventricular myocardium, which did not extend into the left ventricular cavity. The proximal and distal ends of the severed artery were ligated and, then, two mattress sutures were placed in the ventricular laceration. At this stage the blood pressure became obtainable. Next, the pericardium was closed leaving a pleuropericardial window, and the chest was closed after the placement of a drainage tube. The patient then stabilized and underwent an uncomplicated convalescence while the wound healed by primary intention. At no time in his hospital course did the patient complain of precordial pain, except for the sharp pain noted on admission.

Follow-Up.—On follow-up examination, two and one half months after injury, the patient had remained asymptomatic and had returned to work.

DISCUSSION

The electrocardiograms taken before, during, and following the operation are shown in Figs. 1 and 2. The preoperative electrocardiogram was within normal limits. The tracings taken during the operation are considered particularly noteworthy. Except for transient wandering of the atrial pacemaker, the rhythm remained physiologic throughout. The tracings during the opening of the chest and the initial exploration displayed nonspecific S-T-segment abnormalities of low amplitude. Within 3 minutes following the complete ligation of the coronary artery, a pattern of acute anterolateral wall ischemia appeared, but with the cessation of direct cardiac manipulations, this subsided gradually. Subsequent tracings over the period of follow-up showed the progression and disappearance of findings consistent with pericarditis. At no time in any lead has there been evidence of myocardial necrosis.

This patient demonstrates several interesting facets. The diagnostic aids in penetrating wounds of the heart are many. This patient displayed shock, the visible wound in a suggestive area, and a narrowed pulse pressure, but he had no paradoxic pulse, increased systemic venous pressure, distant heart sound,

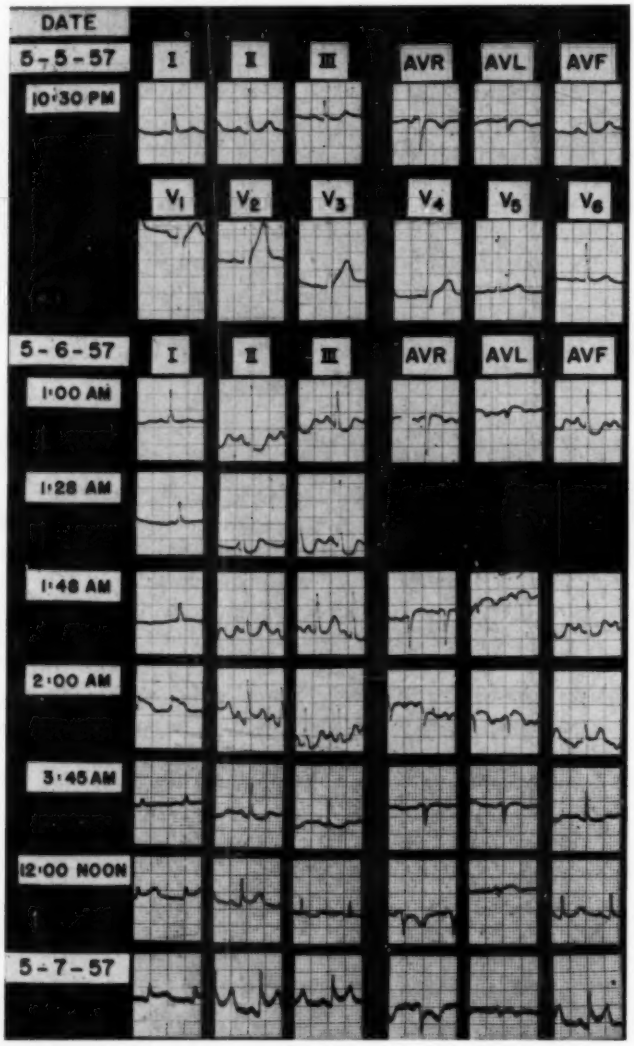

Fig. 1.—Electrocardiograms of J. B. May 5, 1957: 10:30 P.M.: On admission, intoxicated, in shock. May 6, 1957: 1:00 A.M.: Anesthetized, before incision. 1:28 A.M.: Pleura opened, blood pressure 0/0. 1:48 A.M.: Proximal portion of anterior descending coronary artery ligated. 1:50 A.M.: Distal portion of anterior descending coronary artery ligated. 2:00 A.M.: Mattress sutures placed in myocardial laceration. 2:21 A.M.: Blood pressure obtainable. 3:45 A.M.: Skin closed, awakening. 12:00 noon: Awake, alert, incisional and pleuritic pain. May 7, 1957: Comfortable, vital signs stable.

or friction rub, which are so often stated to be helpful in differentiating cardiac from pleuropulmonary lesions. Since the writings of Crastnopol and collaborators,[13] in 1948, preoperative electrocardiograms have been stressed as a diagnostic aid. The preoperative electrocardiogram was within normal limits in this pa-

tient. Despite an obvious left hemothorax, x-ray of the chest on admission did not demonstrate an alteration in cardiac contour. Thus, of the many usual aids to diagnosis, several were absent, and the decision to operate was made because of a deteriorating clinical course.

The literature seldom carefully documents changes due to coronary artery severance. The severity of these lesions is indicated by the work of Chamberlain, Carberry, and Stefko,[14] who found that death occurred in their series of dogs within 15 minutes after division of the anterior descending coronary artery at its origin without ligation, and that with ligation 70 per cent die. Solovay, Rice and Solovay[15] reviewed the electrocardiographic changes in 22 cases of cardiac trauma, and added 1 case of their own. Of these, 8 had ligation of the anterior descending coronary artery. At some point in their course all had QRS changes diagnostic, or strongly suggestive, of infarction. Discussing all 23 cases, they state that the electrocardiographic changes during the first 2 weeks after injury

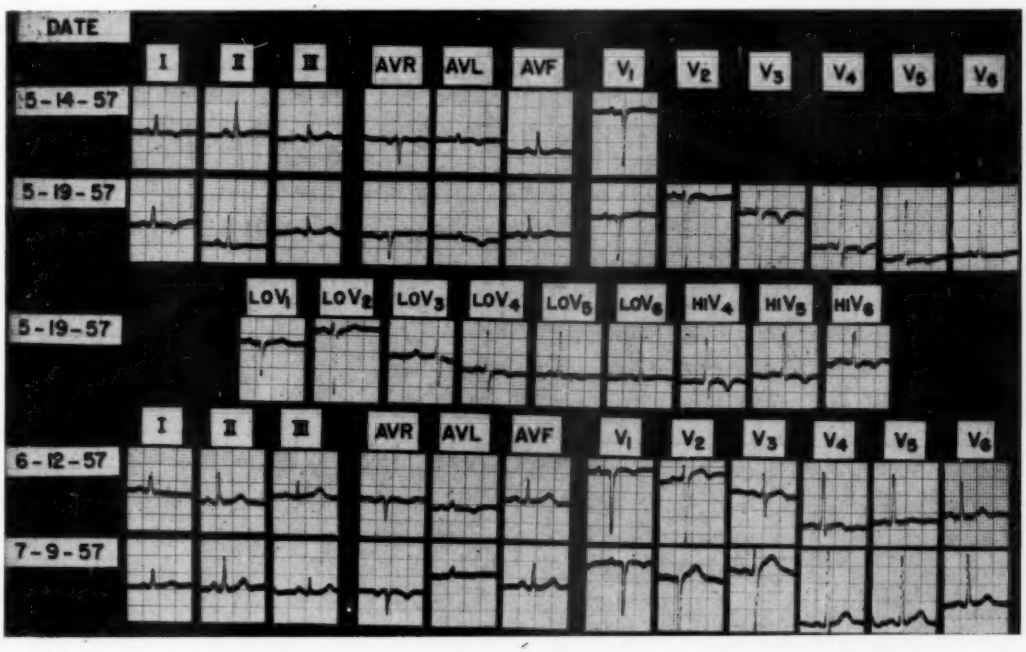

Fig. 2.—Electrocardiograms of J. B. taken during convalescence. Comfortable, progressively ambulated. No symptoms.

always represented pericardial injury, and that after this time they always represented myocardial damage. Griswold and Maguire[7] had 3 cases with coronary artery division out of 27 cases reported. One patient showed "typical anterior coronary block," 1 died before operation from hemorrhage and tamponade, and 1 suffered "typical cardiac dilatation and death on the table" when the coronary artery was ligated. Elkin,[6] in 1941, reported 3 patients who had lacerated anterior descending coronary arteries, all of whom had "typical findings of myocardial infarction"; unfortunately, the electrocardiograms are not described in this report. Many of the studies were limited by the use of only standard limb

TABLE I. CASES OF TRAUMATIC DIVISION OF CORONARY ARTERY

AUTHOR	CASES	LOCATION OF LESION	INFARCTION	COMMENT
Peck[4] (1909)	1	Not specified	Not mentioned whether present or absent	Death after 4 days. No mention of post-mortem findings
Pool[5] (1912)	1	Not specified	Not mentioned whether present or absent	
Purks[17](1931)	1	ADCA in middle third	Present	Standard ECG leads
Porter and Bigger[16] (1932)	1	ADCA in distal third	Not demonstrated	Standard-lead ECGs fail to show infarct
Ramsdell[22] (1934)	1	Not specified	Not mentioned whether present or absent	Death after 1 hour. No mention of findings at post-mortem
Bigger[2] (1939)	1	Small branch of ADCA	Not mentioned whether present or absent in either	ECGs not described
	1	Not specified		
Elkin[6] (1941)	3	ADCA	Present in all	ECGs not shown
Solovay et al.[15] (1941)	8	ADCA	Present in all	Standard-lead ECGs
Griswold and Maguire[7] (1942)	3	ADCA	Present in one	One died preoperatively. One died with cardiac dilatation and arrest when coronary was ligated
Noth[19] (1946)	1	LCA, location not specified	Present	
Graham and Laforet[18] (1952)	2	ADCA at origin in both	Present in both	Post-mortem confirmation
Maynard et al.[8] (1952)	2	ADCA	Not mentioned whether present or absent in any	
	4	RCA		
	1	Small branch		
Carleton and Boyd (1957)	1	ADCA	None demonstrated	

ADCA = Anterior descending coronary artery. LCA = Left coronary artery. RCA = Right coronary artery.

leads with the electrocardiogram. Porter and Bigger[16] reported a case, in 1932, in which the findings in the standard leads failed to show clear-cut evidence of necrosis after division of the anterior descending coronary artery in its distal third. In 1931, Purks[17] reported a case of division of the anterior descending coronary artery in its middle third, with the development of a significant Q wave in Lead III, indicating probable infarction.

With the increased frequency of cardiac surgery, following the popular acceptance of valvular surgery, came the opportunity to study more such cases. Graham and Laforet[18] report 2 cases with careful monitoring of electrocardiograms during and following surgery in which the anterior descending coronary artery was inadvertently ligated. In both of these cases electrocardiographic evidence of infarction appeared, and large infarcts were demonstrated at postmortem study.

Noth[19] has presented the most comprehensive review of the electrocardiographic changes in penetrating cardiac injury. In his series, 1 patient had definite division of the left coronary artery, with a preoperative tracing showing a Q wave in Leads I, II, and III, and an absent R wave in Lead IV_F, with marked S-T-segment elevation in the precordial lead. In 2 other patients with unexplored wounds, changes suggestive of infarction appeared.

The literature reviewed reveals 31 instances in which mention is made of division of a coronary artery. These cases and the results are shown in Table I. No cases were found in which the absence of myocardial infarction was carefully documented. In the present case no evidence of infarction was found despite serial standard and multiple precordial exploring leads.

The reasons for the apparent lack of infarction in this patient are not clear. Blumgart, Schlesinger, and Davis[20] have demonstrated repeatedly by injection of normal hearts the absence of anastomotic channels greater than 40 micra in size in the coronary circulation. However, since the demonstration by Enos, Holmes, and Beyer[21] of gross pathologic evidence of coronary atherosclerosis of varying degree in 77.3 per cent of young soldiers killed in Korea, one may only speculate about the atherosclerotic substratum for anastomosis which may be present in this patient. That functional anastomoses did exist is attested by the vigorous bleeding from the distal segment, and is physiologically shown by the lack of myocardial infarction after complete division and subsequent ligation of the anterior descending branch of the left coronary artery.

SUMMARY

A case of laceration of a major coronary artery with treatment by ligation is presented. Careful electrocardiographic study of this patient failed to demonstrate myocardial infarction. Review of the literature reveals 31 instances of major coronary artery division. In none was the absence of myocardial infarction demonstrated. The reasons for the observed anastomotic coronary circulation in this patient cannot be defined.

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Complications of Left Heart Catheterizations Using the Right Transthoracic Approach

D. Kavanagh-Gray, M.D., and E. H. Drake, M.D., Detroit, Mich.

The usefulness of left-sided cardiac catheterization in the preoperative diagnosis of mitral and aortic valvular disease is well established. In the past, right-sided cardiac catheterizations have been utilized to secure indirect knowledge of left atrial pressures in mitral stenosis. However, the pulmonary capillary pressure tracings have not been adequate for evaluating mitral insufficiency. In the diagnosis of aortic valvular disease, right-sided catheterizations have been useless.

The procedure of left heart catheterization has been utilized since 1952. In that year, J. Facquet[1] published 10 cases of left auricular puncture through the left main bronchus, and H. Engstrom (cited by Björk[2]) obtained left atrial pressure measurements through the esophagus via an esophagoscope. Björk, in 1953, published his technique of left atrial puncture through the right posterior chest.[2,4]

Björk discarded the anterior approach, by which method the needle was introduced into the left ventricle before reaching the atrium, because of the danger of injuring either a coronary artery or the mitral valve, and the danger of producing ventricular fibrillation. The posterior approach from the left side was discarded when it was observed that the needle had to pass through the aorta to avoid the lung. The right transthoracic approach was found to be the most satisfactory, and the procedure has since been adapted to allow for the insertion of a catheter through the needle for access into the ventricle and aorta.[3,5]

Although the usefulness of the procedure has been well established, its degree of safety has not been made entirely clear. Some investigators have felt that the risks were too great and have discontinued its use. Sir Russel Brock,[6] in a series of 24 cases, reported 3 deaths, 5 cases of hemoptysis, 2 of hemothorax, 4 of pneumothorax, and hypotension in most patients who were in left ventricular failure at the time of the catheterization. On the other hand, reports have appeared indicating that the procedure is relatively safe. Out of a total of 490 cases which we have been able to find in the literature there have been 4 deaths (Table I). (Sir R. Brock's previously mentioned series has been omitted.)

From the Division of Adult Cardiology, Henry Ford Hospital, Detroit, Mich.
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TABLE I. COMPLICATIONS OF LEFT-SIDED CARDIAC CATHETERIZATION

SOURCE OF DATA	NUMBER OF CASES	DEATHS	CARDIAC TAMPONADE	HEMO- OR PNEUMO-THORAX	EMBOLI	SERIOUS ARRHYTH-MIA	PNEUMONIA	CATHETER COMPLI-CATIONS
Bagger, Björk, and Malmström[7]	167	1	2	1	1	2	4	2
Lawrence, Zimmerman, Bercu, and Burford[8]	25	0	0	0				1
Fisher[9]	61	0	1	2	0			
Bailey[10]	29	1						
Blakemore (cited by Lawrence[11])	30	1						
Crowley and Parkin[12]	27	0	0	5				
Bougas, Musser, and Goldberg[13]	127	1	0	9	0			1
Brock, Milstein, and Ross[6]	24	3	"Hemoperi-cardium frequent"	6				

Bagger, Björk, and Malmström[7] reported 1 death in their series of 167 cases. Their patient died of cardiac tamponade as a result of inadvertent puncture of an aneurysm of the ascending aorta. Bailey,[10] in a discussion of Fisher's presentation, reported 1 death twenty-four hours after catheterization in a patient with severe mitral insufficiency. "At post mortem, the death did not seem in any way related to the procedure." Bougas, Musser, and Goldberg,[13] in a series of 127 cases, reported 1 death. This again appeared in a patient with mitral regurgitation occurring twelve hours after the procedure. Autopsy did not reveal the cause of death. That these 2 deaths might not have been coincidental with the catheterization cannot be determined. The fourth fatality is mentioned by Blakemore (cited by Lawrence[11]) as being due to hemopericardium, and no further information is available.

It is the purpose of this paper to report our series of left heart catheterizations, to list our complications in detail, and to emphasize the relative safety of the procedure. Since 1955, we have catheterized 113 patients, using the right transthoracic approach to the left atrium. Fifty-eight of our patients were men and 55 were women. The majority of the patients were between 30 and 50 years of age; the youngest was 16 and the oldest 58. All patients were suffering from mitral and/or aortic valvular disease.

METHOD

Each patient was hospitalized and closely observed for 24 hours following the catheterization. If the patient was in congestive failure, several days were spent in the alleviation of symptoms. Penicillin and streptomycin were given in the evening and morning prior to the catheterization, since the needle is known to penetrate the esophagus occasionally. The patient maintained a fasting state for 12 hours, and, if necessary, Seconal, 90 mg., and Demerol, 100 mg., were given on the morning of the procedure in order to allay apprehension. The prone position was assumed by the patient and a suitable site for penetration of the left atrium was determined fluoroscopically. This site was usually near the ninth rib, 4 cm. to the right of the dorsal spinous processes. After anesthetizing the skin, an 18-gauge thin-walled styletted needle, 15 cm. long, was inserted at an angle of 20 to 28 degrees with the vertical in the coronal plane. When the needle was thought to have passed the spine, its position was checked fluoroscopically. When the atrial wall was reached, pulsations were transmitted to the advancing needle, and the wall of the atrium was felt to invaginate for several centimeters before the definite snap of penetration was felt. Pressure tracings were immediately obtained to identify the chamber penetrated.

A small polyethylene or polyvinyl catheter was then threaded through the needle into the auricle, ventricle, and, occasionally, the aorta, and pressure tracings were obtained. Aortic arch pressures were usually obtained by means of an indwelling catheter threaded retrograde through the brachial artery. At the completion of the procedure, the patient was returned to the floor, and blood pressure levels were recorded every 15 minutes for 2 hours, and every 30 minutes for 4 more hours. On the following day posteroanterior and lateral films of the chest were taken.

RESULTS

The average length of time that the needle remained in the left auricle was 49.4 minutes. In 11 patients the left atrium was not entered on the first attempt. In 4 of these 11 patients, the right auricle was penetrated first. Of these 4, 2 had no sequelae; 1 had a small left pleural effusion, seen on the routine postcatheter film, and the fourth developed cardiac tamponade. This last case will be discussed in detail later. In 4 cases, the aorta was entered and the needle immediately withdrawn. One patient was without sequelae, 2 developed asymptomatic pneumothoraxes, as seen on the routine postcatheter film, and 1 developed a mild degree of hypotension several hours later, which cleared without treatment. The needle entered the pulmonary artery in 2 patients and the pulmonary vein in 1, without sequelae. Thus, of the 11 instances in which the needle entered a chamber other than the left auricle, 5, or almost 50 per cent, developed postcatheter complications.

We have listed our complications as minor and major, according to significance. The complications considered as minor were: (1) hypotension, (2) sufficient chest pain to require analgesics, (3) x-ray findings of fluid or air in the pleural cavities, and (4) hemoptysis. Included in the group of major complications were: (1) embolization, (2) cardiac tamponade, (3) serious cardiac arrhythmias (ventricular fibrillation or cardiac arrest), and (4) death.

Minor Complications.—Two patients became hypotensive several hours after the procedure, but recovered without treatment. One patient had a vasovagal attack at the completion of the catheterization. The blood pressure fell from 105/45 to 75/25 mm. Hg, but returned after intravenous therapy of 5 per cent glucose in water was instituted.

Nineteen patients felt that they had sufficient chest pain to require analgesics. In most cases the pain was at the site of the needle puncture, but occasionally true pleuritic pain occurred. Two patients complained of a pain on swallowing, which cleared spontaneously.

One hundred and eleven of the 113 patients had roentgenograms of the chest twenty-four hours after the catheterization. In 8 cases a small amount of fluid or air appeared in one or the other of the pelural cavities. Treatment was unnecessary, and only 1 of these patients complained of chest pain on deep inspiration.

Hemoptysis occurred in 2 patients within twenty-four hours after catheterization, but cleared spontaneously.

Major Complications.—One patient unquestionably developed embolic phenomena following left atrial puncture. Twenty-four hours after a difficult catheterization (the needle was in the atrium 100 minutes, and its position changed three times to allow for insertion of the catheter into the ventricle), he developed a cold, painful, and numb right index finger. Several days later the left atrial puncture was repeated, with the needle remaining in the atrium for 75 minutes. Twenty-four hours later he complained of severe pain in the left upper abdomen, followed by a slight fever, and the demonstration of a tender, palpable spleen.

A second patient developed embolic occlusion of the left middle cerebral

artery forty hours after an uncomplicated catheterization. This patient had aortic valvular disease and had been fibrillating until his conversion to regular rhythm with quinidine twenty-four hours prior to the catheterization.

We have had one case of pericardial tamponade. The patient was a 16-year-old girl who came for a combined right and left heart catheterization. She was subjected to a routine right-sided catheterization, and with the catheter still in the right atrium, a left transthoracic atrial puncture was attempted. Unfortunately, this procedure was difficult and time-consuming, because the needle twice entered the right atrium. That evening, because of complaints of retrosternal pain and thirst, and because of the findings of tachycardia, absent blood pressure, and pericardial friction rub, a diagnosis of cardiac tamponade was made. After a diagnostic pericardial paracentesis revealed gross blood, decompression of the pericardium was carried out. The patient made an uneventful recovery.

This case represents a serious complication which, however, cannot be attributable solely to the left catheterization. She had a combined catheterization, and the heparin received through the right catheter during the long procedure most certainly contributed to the bleeding.

Blood-tinged pericardial fluid is seen at surgery in approximately three fourths of the patients after left heart catheterization. This fluid is not under pressure and seemingly causes no symptoms. There have been no deaths or serious cardiac arrhythmias in the series.

SUMMARY

We have reported the complications encountered during our series of left heart catheterizations. Of the 113 patients catheterized, hypotension developed in 3, sufficient chest pain to require analgesics was present in 19, hemoptysis appeared in 2, and routine, 24-hour chest roentgenograms revealed air or fluid in a pleural cavity in 8. In 3 instances, major complications have occurred in the form of embolic phenomena and cardiac tamponade. There have been no deaths.

The incidence of complications has been significantly higher in cases in which the left atrium was not entered on the first attempt. It has been our impression, and that of other investigators, that puncturing the base of the aorta carries the greatest risk.

The safety of the procedure, as carried out here, compares favorably with that of other investigators. It is our conclusion, therefore, that left heart catheterization, utilizing the right transthoracic approach to the atrium, is sufficiently safe to use in cases of diagnostic problems involving the aortic or mitral valves.

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Book Reviews

MECHANISMS OF HYPERTENSION: WITH A CONSIDERATION OF ATHEROSCLEROSIS. By Henry Alfred Schroeder, M.D., Springfield, Ill., 1957, Charles C Thomas, 379 pages. Price $9.00.

In the first half of this monograph Dr. Schroeder presents his current views on the mechanisms responsible for the initiation and evolution of primary hypertension. He accepts heredity as one of the basic predisposing factors and believes that the characteristic which is inherited is "a tendency to react to stress by vasospasm." On the basis of the assumption that hypertension is largely confined to civilized people, it is suggested that the environmental stresses which initiate the disease in predisposed individuals are those which are inherent in an industrialized society. The existence of a specific defect of personality in hypertensive individuals is regarded as not clearly established, but it is conceded that there are important emotional factors in the disease which may be either primary or secondary.

The consensus of the conflicting evidence in the literature is judged to be strongly in favor of the hypothesis that the "vasospasm" which occurs during the early stage of intermittent or highly variable hypertension is mediated through overactivity of the sympathetic nervous system. In the later stages of the disease these neurogenic factors are gradually replaced by other mechanisms which are capable of maintaining more or less permanent vasospasm. On the basis of a review of the evidence which has been adduced in support of various hypotheses concerning the nature of these perpetuating mechanisms, it is concluded that the most important are those which originate in the kidneys as a result of renal ischemia induced by neurogenic vasoconstriction.

Several ways in which renal ischemia might give rise to a generalized pressor effect are discussed; for example, inhibition of amine oxidase might be expected to increase the amount of circulating pressor amines. This is an attractive hypothesis, but the author rejects it on the grounds that the concentration of pressor amines detectable in the blood of hypertensive patients is too low to explain the observed increase in peripheral resistance. It is considered possible, however, that inhibition of amine oxidase might decrease the rate of destruction of certain pressor polypeptides of renal origin, such as hypertensin and pherentasin.

Another group of hypotheses concerning the nature of nephrogenic pressor mechanisms is based on the ability of hydralazine to lower the blood pressure of hypertensive patients and the assumpton that it may do so by virtue of its known ability to bind heavy metals. In an attempt to suggest a mechanism whereby metal binding might produce an antihypertensive effect, evidence is cited to show that there is a progressive increase with age in the concentration of certain abnormal trace metals in the tissues of Americans, but not in those of primitive peoples.

It is suggested, for example, that accumulation of cadmium in the kidney might replace an essential trace metal in a metalloenzyme such as dihydroxyphenylalanine decarboxylase or monamine oxidase, with resulting inhibition of the enzyme. If one assumes that the inhibition of these or other enzyme systems is a mechanism whereby hypertension is sustained, the antihypertensive action of hydralazine could be explained on the basis of its ability to reverse the inhibition by chelating the abnormal trace metal.

An even more speculative hypothesis which is discussed in several places in the book is the possibility that a localized deficiency of vitamin B_6 might be produced in the kidney as a result of interference with an essential trace metal by an extraneous one, even in the absence of signs of a general deficiency in the body as a whole. The only evidence cited in favor of this hypothesis is the fact that an elevation of blood pressure can be produced in young rats by administration of a vitamin B_6 antimetabolite.

The role of the adrenals in the pathogenesis of hypertension is discussed briefly, but the author does not believe that overactivity of the adrenal cortex occurs in the great majority of cases of hypertension. He dismisses the finding of increased amounts of aldosterone in the urine of some hypertensive patients as merely an example of secondary aldosteronism due to some defect in the handling of sodium by the kidney.

The chapter on the pathogenesis of atherosclerosis is included partly because of the importance of coronary and cerebral atherosclerosis as a cause of death in hypertensive patients, and partly in order to present the hypothesis that abnormal trace metals and a deficiency of vitamin B_6 may be important pathogenetic factors in atherosclerosis as well as in hypertension. Since a deficiency of pyridoxine has been shown to cause damage to subintimal mucopolysaccharides in the monkey, it is postulated that a "conditioned" deficiency of vitamin B_6 localized in the vessel wall might be a factor in the initiation of human atherosclerosis. On the basis of experiments in rats, a deficiency of vitamin B_6 might also be expected to favor the development of atherosclerosis by interference with the desaturation of fatty acids. It is also suggested that the accumulation of abnormal trace metals, chromium for example, might exert an atherogenic influence by stimulating the formation of cholesterol and fatty acids in the liver.

The last chapter in the book describes a proposed regimen for the treatment of atherosclerosis which is based on the above concepts of pathogenesis. The method includes the use of a diet which is low in animal fats and in saturated fatty acids generally, and which is high in unsaturated fats, especially linolenic acid. In addition, the patient is given a daily dose of 5 or 10 mg. of vitamin B_6 and 0.5 Gm. of the chelating agent, calcium Versenate, to remove any abnormal trace metals which may be present. It is admitted that this form of therapy has not been employed long enough to permit evaluation of its effectiveness, but the early results are said to be encouraging. There is also a chapter on the treatment of hypertension which merely summarizes Dr. Schroeder's previously published experience with the intensive use of the combination of ganglionic blocking agents and hydralazine.

The author's admitted objective in writing this monograph is to put forward hypotheses which he believes to be in accord with the existing evidence, in the hope that they will stimulate controversy. In order to do this, much evidence from the literature has been accepted at its face value without critical examination of its validity, and in many instances support for a given hypothesis has been drawn from experimental observations whose relevance to the problem under discussion is distinctly limited. Nevertheless, all those who are engaged in the study of the pathogenesis of hypertension will find this monograph full of thought-provoking speculations concerning the interplay between some of the little understood physiological and biochemical factors which may be involved in the regulation of the blood pressure.

K. A. E.

L'ANNEE CARDIOLOGIQUE INTERNATIONALE, TOME V (The International Yearbook of Cardiology, Vol. V). Edited by Camille Lian, Paris, 1956, Expansion Scientifique Française, 374 pages.

This fifth volume in its series assembles 24 articles written by French and other European cardiologists and is edited by Professor Camille Lian. It would not be practical to review each article, but as a whole the volume is a useful one which rewards the reader with precise information on a variety of subjects. Some of the articles merit special mention: "Pregnancy and Cardiopathies in 1955," by P. Broustet, of Bordeaux. "Abnormalities of the Pulmonary Arteries in Cases of Mitral Stenosis Due to Undergo Commissurotomy," by G. C. Dogliotti, of Turin. "The Late Results of Mitral Valvulotomy," by E. Coelho and J. F. DaCosta, of Lisbon. "The U Wave of the Clinical Electrocardiogram," by Max Holzmann, of Zurich. "Ebstein's Syndrome," by M. Mauquin, of Paris. "The Direct and Indirect Effects of Salicylate Therapy," by Jacques Roskam, of Liege. "Primary Pulmonary Arterial Hypertension," by P. Soulié, of Paris.

This book offers an excellent view of the evolution of cardiology in Europe. Professor Lian deserves much credit for his wise editorial guidance. This book is highly recommended to all interested in cardiology.

H. S.

HYPOTENSIVE DRUGS. Edited by M. Harington, London, 1956, Pergamon Press Ltd., 221 pages. Price $8.00.

This volume contains the proceedings of a symposium on hypotensive drugs and the control of vascular tone in hypertension which was held in April, 1956, under the auspices of the Biological Council's Coordinating Committee for Symposia on Drug Action. Twenty-two speakers from the United Kingdom and from five foreign countries participated in the symposium, which was organized in four sessions dealing with the chemistry, pharmacology, and clinical applications of hypotensive drugs and with factors involved in the control of vascular tone in hypertension.

The first section of the book deals with the chemistry and structure-activity relationships of most of the common classes of hypotensive drugs, special emphasis being placed on the ganglionic blocking agents. Considerable progress is being made in the understanding of the structural characteristics of secondary, tertiary, and quaternary bases which determine such important pharmacologic attributes as ease of absorption from the intestine and relative activity of blockade at sympathetic and parasympathetic ganglia.

Much of the discussion in the pharmacologic section concerns the mode of action of reserpine, especially the significance of the fact that it stimulates the release of 5-hydroxytryptamine from the intestine, from the blood platelets, and from the brain. There seems to have been general agreement that an increase in circulating 5-hydroxytryptamine may well be the cause of some of the side-effects of reserpine but is probably not responsible for the hypotensive effect. The existence of true synergism between reserpine and other hypotensive agents was regarded as still unproved.

An interesting suggestion concerning the mechanism of development of tolerance to the hypotensive action of ganglionic blocking agents is made by Dr. Eleanor Zaimis. She reviews the results of experiments which indicate that ganglionic blocking agents may also act peripherally to sensitize arteriolar smooth muscle to the vasoconstrictor effect of epinephrine and norepinephrine.

In the section on clinical applications of hypotensive drugs, Professor McMichael gives a guardedly optimistic review of the results achieved in a series of 62 cases of malignant hypertension treated with subcutaneous hexamethonium or pentolinium during the preceding 5 years. Professor Smirk expresses a preference for oral therapy with pentolinium and reserpine. He appears to be enlarging his indications for this form of therapy to include not only patients with Keith-Wagener Grade 3 and 4 fundi, but also most patients with hypertensive symptoms and even some of the asymptomatic cases with only moderately increased blood pressure levels. Dr. George Perera enters a plea for the use of adequate data on untreated controls as a basis for evaluation of the effects of drug therapy on patients who are not in the accelerated phase.

The final section deals with the control of vascular tone in hypertension. Professor Clifford Wilson presents the evidence which has led him to believe that there is a common physiologic mechanism underlying all forms of persistent hypertension, regardless of the nature of the initiating factor in the early stage. This common factor is probably a change in the chemical environment of arteriolar smooth muscle which leads to a change in its responsiveness. Dr. Björn Folkow offers a mechanical explanation of the way in which hypertrophy of the smooth muscle layer of the arteriolar wall may be responsible for an increase in peripheral resistance, even in the absence of organic narrowing of the lumen by arteriolar sclerosis.

The discussion of the mechanisms involved in experimental renal hypertension reflects the difficulties which have arisen in connection with some of the established concepts as a result of the discovery of renoprival hypertension. No completely satisfactory hypothesis has been put forward to provide a common mechanism for the hypertension produced by unilateral renal artery constriction and that caused by bilateral nephrectomy. The hypothesis which seemed to receive most support in this symposium was the suggestion that the fundamental role of the kidney may be to maintain normal blood pressure by regulating some extrarenal pressor mechanism, possibly one of adrenal cortical origin.

This is a book which should be in the library of everyone who is actively engaged in the study of pathogenetic mechanisms in hypertension. Its virtues lie not only in the thoughtful presentations of various points of view by the principal speakers, but also in the verbatim reports of the excellent general discussion which took place at the end of each session.

K. A. E.

LA CARDIOPERICARDIOMYOPEXIE (Cardiopericardiomyopexy). By Professor C. Lian, A. N. Gorelik, and Mendel Jacobi, Paris, 1956, Expansion Scientifique Française, 102 pages.

This reviewer cannot understand why Professor Lian undertook to "father" the publication of this monograph which contributes nothing to the progress of either French or American cardiology. The value of cardiopericardiomyopexy, which had its beginnings in 1938, would interest us more if Professor Lian himself had controlled the selection of cases and followed their postoperative progress.

The monograph is made up of 3 chapters. The first deals with principles of diagnosis related to cardiovascular diseases which lend themselves to treatment by cardiopericardiomyopexy. Professor Lian reviews the principal signs and symptoms of angina pectoris, coronary thrombosis, and mitral and aortic valvular diseases. In the second chapter, Dr. Aron Gorelik, of New York, describes the surgical procedure and discusses his results. Magnesium silicate is introduced into the pericardial cavity to bring about inflammatory fusion of its two layers, and pectoral muscle is attached to parietal pericardium. In 100 cases followed for 7 years, the results reported are as follows: operation mortality in 5 per cent, postoperative mortality in 10 per cent, and excellent clinical relief of symptoms in 85 per cent. Apparently all the survivors lead absolutely normal lives. Either these results are exact and all patients with angina pectoris should be operated on in this manner, or they require more critical evaluation. The descriptions of cases cited are too brief to be convincing.

Fifty cases of rheumatic valvular disease were treated by this surgical technique since January, 1951; the operation mortality was 12 per cent and the postoperative mortality, 8 per cent. "The remaining 40 cases presented spectacular improvement. Whereas dyspnoea prevented any physical effort before operation, they all resumed their usual occupations and enjoyed their work after the operation." Obviously, the author does not take into account the subtleties of clinical medicine when he recognizes only death or perfect well-being as the possibilities.

In the third chapter, Dr. Mendel Jacobi, of New York, describes observations on the anatomic lesions of the myocardium and coronary arteries in 3 cases, 2 of myocardial infarction and 1 of acute rheumatic fever. These studies are, we think, too small in number to justify any general conclusions concerning a technique such as cardiopericardiomyopexy.

This monograph does not present a convincing case for the surgical procedure it recommends.

H. S.

LE VOLUME SANGUIN DES POUMONS CHEZ L'HOMME. By Jacques Lammerant, Brussels, 1957, Editions Arscia, 192 pages.

This volume records in considerable detail the investigations of the author on the measurement of the volume of blood existing at any one time in the lesser circulation. The technique developed by the author and his associates consists in the plotting of a flow curve of radioactive I^{131} albumin injected into an arm vein. The scintillation counter is very carefully positioned over the chest after a fluoroscopic study of the position of the heart. The curve of traverse of the radioactive material is analyzed by Stewart's technique.

The first 55 pages of this monograph are devoted to a detailed discussion of different experimental techniques and their validity under different conditions. The author's findings in normal subjects agree closely with those found by others using similar techniques, namely, that the lesser circulation contains approximately 25 per cent of the total blood volume. He confirms that in the basal state there is no close correlation between the cardiac output and the volume of blood in the lungs, but finds that the increase in cardiac output which occurs during exercise or in the postdigestive state is associated with a definite decrease in the pulmonary blood volume. The differences he has demonstrated appear to be statistically significant. A third chapter is concerned with the study of a group of 25 patients with mitral stenosis of varying severity. His conclusions agree with those reported by others that the pulmonary blood volume does not differ appreciably from that found in normal subjects under similar conditions, provided that the total blood volume is not significantly different from normal. No correlation could be found between the volume of

blood contained in the lungs and the pulmonary artery pressures or the degree of pulmonary congestion as judged by clinical signs. Two patients with mitral stenosis were studied during exercise, with differing results, and it is doubtful if these two observations can be regarded as of much significance.

The author is very well aware of all the previous work that has been done in his field, and there is an excellent and complete bibliography of the subject. Furthermore, there is a very useful critical analysis of methods, and the results obtained by his technique are compared to those by other authors. One of the features of the lesser circulation which is difficult to grasp is that although the total volume of blood in pulmonary arteries, arterioles, capillaries, and veins is of the order of 1.2 liters, only about 60 c.c. of this blood is actually in pulmonary capillaries at any one time. The author fully accepts the experimental work by Roughton, who showed that the volume of blood exposed to alveolar gas at any one instant is as little as 60 c.c., and he devotes some space to speculative thought as to where the remainder of the blood is situated. The wide discrepancy between the volume in the capillaries and the volume in the lesser circulation as a whole makes it easy to understand why pulmonary congestion at the capillary level (where it will presumably exert its greatest effect on pulmonary compliance) may be caused by perhaps the addition of only 60 c.c. more blood than normal in this situation. The technique that the author has used would clearly not be capable of detecting a difference as small as this, and he shows that he is well aware of this difficulty.

This monograph is excellently written, and although it has a rather inadequate summary in English, the many tables repay a careful study by those interested in this field who do not feel able to translate the text for themselves. Fortunately, all the relevant data is excellently presented in the tables, and a minimal knowledge of French is required to extract from them the interesting and valuable information they contain. This monograph is undoubtedly essential reading for all those concerned in understanding the lesser circulation, and in trying to visualize what, in hemodynamic terms, can be the meaning of words such as "pulmonary congestion" which have passed into common currency without being subjected as yet to really detailed critical analysis.

D. B.

PHARMACOLOGIC PRINCIPLES OF MEDICAL PRACTICE. By John C. Krantz, Jr., and C. Jelleff Carr, Ed. 4, Baltimore, 1958, Williams and Wilkins Company, 1313 pages.

Any book that is in its fourth edition must have sufficiently wide appeal to convince the authors to go through the backbreaking, time-consuming job of revision. Krantz and Carr have not only brought their book up to date in this revision but have added a considerable amount of new material. The rapid progress of pharmacology is indicated by the fact that 140 new drugs are described, and new chapters on psychopharmacology and drugs used locally in the ear, nose, and throat have been added.

The text is clearly written, but at times, in an attempt to avoid discussion of controversial material, is dogmatic. However, this book has been written primarily for medical students, and those who wish to delve more deeply into any particular subject have available at the end of each chapter a selected list of references. The therapeutic implications are given, but this book is in no sense a textbook of therapeutics. The authors have followed the custom of previous editions by including photographs of eminent pharmacologists. Diagrams and illustrations are placed where necessary. An excellent feature is the listing of the U.S.P. and N.F. preparations and dosages at the end of each chapter. The authors established a principle of using what they consider the common name of a drug—sometimes this is the generic name and at other times, the trade name. No attempt is made in the text to indicate when a trade name is used. It would be of help to the reader if, in future editions, the standard symbol, ®, were placed after the trade name.

Although this book is designed for medical students, it is also a good reference book on modern pharmacology for the practicing physician.

A. DeG.

CLASSICS IN ARTERIAL HYPERTENSION. By Arthur Ruskin, M.D., Springfield, Ill., 1956, Charles C Thomas, 358 pages. Price $9.50.

This book is composed of selected publications (translated into English where necessary) of investigators whose contributions are milestones in the history of arterial blood pressure.

A brief and amusing introductory chapter deals with pulse-lore, and this is followed by a history of the methods of measuring blood pressure. This begins with the work of Stephen Hales (1733), who measured intravascular pressures in animals much as one measures the cerebrospinal fluid pressure of patients today. There follows the investigations of Poiseuille, who adapted the mercury manometer to the measurement of intravascular pressures; the project was carried out and published while Poiseuille was still a senior medical student in Paris. After dealing with other significant contributions, this section culminates in the 1905 publication of Korotkov on the auscultatory method of measuring systolic and diastolic blood pressures as currently employed.

In the chapters entitled "Significance" one encounters the paper of Richard Bright, correlating sclerosis of the kidneys with hardness and fullness of the pulse. This paper was published in 1827, one year before that of Poiseuille which dealt with the manometric measurement of intravascular pressure. On the basis of Bright's work, hypertension was regarded as being entirely of renal origin, and it was not until the turn of the century that the present concept of primary and secondary hypertension evolved. When one realizes that some seven decades elapsed between the publications of Bright and Poiseuille and the development of the first clinically acceptable sphygmomanometer by Riva-Rocci (1896), one can appreciate the difficulties that faced the mid-nineteenth century clinicians and pathologists in their efforts to unravel the interrelationships of hypertension, renal disease, and arteriosclerosis.

The closing chapters are comprised of papers dealing with the etiology of hypertension. The first one is by Tigerstedt and Bergman (1897), and describes their discovery of the pressor activity of renal extracts; the final one, appropriately enough, is Goldblatt's (1934) treatise on the production of experimental renal hypertension.

This book will intrigue those whose main concern is the field of hypertension, and will be equally appealing to those interested in the experimental method and clinical observation.

B. A. L.

THE CLINICAL ASPECTS OF ARTERIOSCLEROSIS. By Seymour H. Rinzler, M.D., Springfield, Ill., 1957, Charles C Thomas, 339 pages. Price $8.75.

The author's principal objective in writing this monograph is to summarize the extensive and widely scattered literature on the clinical aspects of arteriosclerosis for the guidance of the general practitioner who is frequently confronted with such problems.

The term arteriosclerosis is defined in a generic sense to include atheromatosis, atherosclerosis, Mönckeberg's sclerosis, and hyperplastic (involutionary) arteriosclerosis, but almost all the detailed discussion in the book concerns atherosclerosis, and the terms arteriosclerosis and atherosclerosis are often used more or less interchangeably throughout the text.

The first chapter, which lists nearly 300 references to the literature, deals with the incidence of arteriosclerosis and summarizes current ideas on the role of various factors in the etiology and pathogenesis of the condition. This chapter is somewhat disappointing because it is neither long enough to supply the sophisticated reader with a comprehensive summary of all the conflicting points of view, nor short and critical enough to provide authoritative guidance for the reader who is merely searching for a reasonable, provisional attitude which he may use as a guide in clinical practice, pending clarification of the disputed issues by future research.

The next seven chapters are devoted to a discussion of the clinical manifestations, diagnosis, and treatment of coronary heart disease. Apart from the more liberal use of references to the literature, this section of the monograph follows the conventional pattern of a chapter on coronary heart disease in a textbook of cardiology. Chapters on the treatment of congestive heart failure and on drug therapy of disorders of the heart beat are also included in this section, but, as might have been expected, it was not possible in a monograph on arteriosclerosis to allocate sufficient

space to permit adequate coverage of subjects such as these which have no specific relation to coronary heart disease. In a textbook of cardiology, on the other hand, it is possible to present a single, comprehensive discussion of congestive heart failure, so that in the chapters on individual diseases only those aspects of heart failure which are specific to the disease in question need be mentioned.

Nearly half of the chapter on the cerebral aspects of arteriosclerosis is devoted to a discussion and tabulation of the neuroanatomic basis of the symptoms and signs produced by occlusion of individual arteries which supply blood to the brain and spinal cord. Perhaps as a result of the limitations imposed by the title of the monograph, cerebrovascular accidents are discussed with only incidental reference to the role of hypertension and arteriolar sclerosis. This is unfortunate because hypertension plays an important and sometimes dominant role in the great majority of strokes in patients under 60 or 70 years of age. Moreover, the presence of an elevated blood pressure is often the most important single factor which influences decisions regarding treatment and prognosis.

The remainder of the book consists of short chapters on the clinical aspects of aortic, peripheral, retinal, renal, and pulmonary arteriosclerosis. In several places in this section limitations of space seem to have made it impossible to present an adequate discussion of points of considerable importance in everyday practice. For example, the short paragraph which deals with the ophthalmoscopic characteristics of retinal arteriosclerosis with and without hypertension is particularly unsatisfactory and even confusing. On the other hand, in the chapter on arteriosclerosis of the aorta, two pages are devoted to a detailed description of the technique of aortography, a procedure which is rarely performed except by specialists in the field of vascular disease.

In view of the contradictory nature of much of the material which is cited from the literature without critical comment, it is unfortunate that a summary was not given at the end of each chapter in order to permit the author to express his personal evaluation of the consensus of the available evidence. A minor, but rather irritating shortcoming of the book, which is otherwise beautifully printed and illustrated, is the frequency with which errors of spelling and composition have escaped correction by the proofreader.

Dr. Rinzler deserves to be congratulated for having summarized in a single volume such a large cross section of the literature on the clinical aspects of arteriosclerosis, since this material would otherwise have remained scattered throughout a very large number of books and periodicals dealing with various specific manifestations of the condition. It is this reviewer's opinion, however, that this monograph is likely to be of a greater value as a source of ready reference for those whose special interests lie in the field of arteriosclerosis than as a practical manual for day-to-day use by the general practitioner.

K. A. E.

ANAESTHESIA (BRITISH MEDICAL BULLETIN). Vol. 14, No. 1, January, 1958. Published by Medical Department, The British Council, London, 72 pages. Price £1 or $3.25 post free.

Volume 14, Number 1 of this Journal is a symposium containing short, essentially practical articles mainly of interest to the anesthetist, but with papers for those whose study is in cardiology and respiratory function. It contains no very academic papers but is based on the observations and thinking of experienced men.

Professor Whitteridge describes the effects, and consequences, of volatile anesthetics and other drugs on the sensitivity of the stretch receptors in the lung and those of the carotid and aortic pressor receptors. Professor Pask details many of the factors governing and relating to CO_2 levels in anesthesia and the effects of the variation in mechanical factors on the exchange of gases in the lungs and tissues. He also points out the difficulties in assessing the effects of CO_2 on human beings by the interpretation of animal experiments.

Lucas, in his article on hypothermia, recalls the stimulus of modern cardiac surgery on the concept originally used by Bayle and Currie in the eighteenth century. He deals in some detail with the occurrence and treatment of the variety of cardiac arrhythmias which have been found to occur in this form of therapy.

The advantages and disadvantages of hypotensive anesthesia are laid before the reader by different authors, each being convinced of his argument. The factors leading to respiratory inadequacy are outlined, with methods of assessing pulmonary ventilation and treatment of its inadequacy in certain diseases, including a paragraph on the controversial subject of narcotic poisoning.

Those sections of particular interest to the anesthetist include a detailed account of rebreathing systems in anesthetic apparatus and the ideals to be sought in such systems; and the biochemical disturbances in the body covering each regulating mechanism in turn.

This short but easily read Journal brings to its readers a synopsis of the more recent thought on a fair range of subjects and is worth reading.

R. G. B. G.

CLINICAL ELECTROCARDIOGRAPHY—INTERPRETATION ON A PHYSIOLOGIC BASIS. By Manuel Gardberg, M.D., New York, 1957, Paul B. Hoeber, Inc. Price $12.75.

As the presentation of a method of interpretation this book offers no new points of view, the electrical effects of depolarization and repolarization, and the alterations of disease processes being described as in many other texts on the subject. At times this same point of view seems to be made unnecessarily complex. There are numerous detailed drawings accompanying the descriptive material, many of which are so complex as to be distracting. Moreover, they are often annoyingly separated by several pages from the related descriptive material, necessitating much shifting of attention as well as pages.

There are also several omissions or near omissions from the book. Peri-infarction block is not discussed, although a good example is presented in Fig. 167b. More detailed discussion of the ECG effects of congenital heart disease would have been useful in view of recent advances in this area. The causes and significance of left and right axis deviation are never discussed as a unified section. For reasons which are not clear, the ECG effects of pleural and pericardial effusion are discussed under right ventricular hypertrophy.

The book seems to have little to offer for the experienced reader, and is unnecessarily complex for the beginner.

E. H. E.

THE PHYSIOLOGY OF INDUCED HYPOTHERMIA (NAS-NRC publication, 451). Edited by Robert D. Dripps, Washington, 1957, National Research Council.

This book is a report of the proceedings of a symposium convened by the Division of Medical Sciences, National Academy of Sciences, under the chairmanship of Dr. R. D. Dripps, who also edited this publication. It is composed of five parts: General Physiochemical and Physiologic Considerations of Hypothermia; The Effects of Hypothermia on Specific Systems; Myocardial Irritability and Hypothermia; Clinical Application of Induced Hypothermia; Techniques of Inducing Hypothermia.

Direction of the symposium was controlled by subcommittees on anesthesia, the cardiovascular system, shock and trauma.

Since every system and microsystem of the body is affected by hypothermia, this book is filled with detail of a hypothetical, experimental, and practical nature. The majority of the participants have had considerable experience in the experimental field.

Animal studies in relation to hibernating and nonhibernating species and their differing physiologic responses are outlined. Special emphasis is laid on pulmonary ventilation, blood gases, oxygen utilization, plasma pH, electrolyte balance, and cardiac output.

Hypothermia as it affects each different system is discussed most fully, especially as it concerns the cardiovascular and central nervous systems. Liver function, renal function, hematological changes, and pituitary adrenal responses are reported in detail.

Because the range of hypothermia is so dependent upon the cardiac response, a complete section is devoted to the behavior of the heart. It is concluded that up to the onset of fibrillation enough oxygen is carried to the heart muscle and adequate carbon dioxide is eliminated. At

this stage the many physiochemical changes, both gross and minute, which play a role in increasing the irritability of the muscle are reported. Of interest are the different results obtained by different investigators.

The clinical uses of hypothermia are reviewed in relation to neurosurgery, cardiac surgery and hemorrhagic shock. The associated use of autonomic blocking agents and other drugs are reviewed, as is the anesthetic management of cases undergoing hypothermia.

Much of the material in this book has been published elsewhere, but it is most convenient to have it compiled within one volume. The bibliography is most complete. A vast amount of work is reported in this book, and many of those who report it feel that there is still much more work to be done in this field.

This book should certainly be at hand for all those interested in the investigational or clinical uses of hypothermia.

R. G. B. G.

Announcements

THE SIXTEENTH INTERNATIONAL CONGRESS OF THE HISTORY OF MEDICINE will be held at the Faculty of Medicine, Montpellier, from Sept. 22 to 28, 1958, under the general direction of M. Giraud, dean of the faculty.

Registrations are now being accepted by Professor Turchini, President of the Organization Committee, Faculty of Medicine, Montpellier (Hérault), France.

The following subjects have been selected for consideration: (1) Relationship between the School of Montpellier and the medical institutions of various countries through the centuries. (2) History and growth of hospital establishments. (3) Medical iconography during the seventeenth century. (4) The New World's contribution to therapeutics. (5) Miscellaneous.

The registration fees are as follows: 6,000 francs (French) for nonmembers of the History of Medicine Society; 4,000 francs (French) for members; and 3,500 francs (French) for guests.

The Organization Commitee would appreciate having as early as possible the titles of the communications which are to be presented (10 minutes for each), as well as a short abstract.

Remittances may be made by check to either of the following:

Compagnie Algérienne de Montpellier No. W12-900-3.

Compte courant Postal Montpellier No. 1178-03 (XVI Congrès International d'Histoire de la Médecine, Faculté de Médecine, Montpellier).

THE LIFE INSURANCE MEDICAL RESEARCH FUND is now receiving applications for MEDICAL RESEARCH FELLOWSHIPS AND GRANTS to be available July 1, 1959, as follows: (1) *Until Oct. 15, 1958*, for postdoctoral research fellowships. Candidates may apply for support in any field of the medical sciences. Preference is given to those who wish to work on fundamental problems, especially those related to cardiovascular function or disease. Minimum stipend is $3,800, with allowances for dependents and necessary travel. (2) *Until Nov. 1, 1958*, for grants to institutions in aid of research on cardiovascular problems. Support is available for physiological, biochemical, and other basic work broadly related to cardiovascular problems as well as for clinical research in this field.

Further information and application forms may be obtained from the Scientific Director, Life Insurance Medical Research Fund, 345 East 46th Street, New York 17, N. Y.

A COURSE IN ELECTROCARDIOGRAPHIC INTERPRETATION FOR GRADUATE PHYSICIANS will be given at the Michael Reese Hospital by Louis N. Katz, M.D., and Alfred Pick, M.D., and associates. (Dr. Katz and Dr. Pick are Director and Associate Director, respectively, of the Cardiovascular Department.) The class will meet daily from 9:00 A.M. to 5:00 P.M., August 18 through August 30.

Further information and a copy of the lecture schedule may be obtained upon application to Mrs. Margaret Stern, Administrative Secretary, Cardiovascular Department, Medical Research Institute, Michael Reese Hospital, Chicago 16, Ill.

The Third Annual Volume of the BIBLIOGRAPHY OF MEDICAL REVIEWS was published in June, 1958.

Review articles listed in Volumes 1 and 2 are a by-product of the *Current List of Medical Literature* and were duplicated in the parent publication in another format. With Volume 3, however, the collection of review articles was extended to all of the current journals received by the National Library of Medicine. The result has been the inclusion in Volume 3 of approximately 600 non-Current List articles along with 2,300 review articles also listed in the Current List.

The 1958 volume of the *Bibliography of Medical Reviews* is arranged by subject, with a separate author index, and contains approximately 2,900 references to review articles in clinical and experimental medicine and allied fields which have appeared largely in 1957. Copies of Volume 3 for 1958, are available from the Superintendent of Documents, U.S. Government Printing Office, Washington 25, D.C.

Erratum

In the article entitled "Ventricular Pre-Excitation (WPW) in the Presence of Bundle Branch Block," by Alfred Pick, M.D., and Charles Fisch, M.D., in the April, 1958, issue of the JOURNAL, pp. 504-512, the calculated chance incidence given in line 8 on page 504 should read 0.0024 per cent instead of 0.24 per cent.